GUIDE

TO THE

EXAMINATION OF URINE,

WITH SPECIAL REFERENCE

TO THE

DISEASES OF THE URINARY APPARATUS

—BY—

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SECOND EDITION.

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PREFACE.

In bringing this little work before the medical public, the translator has been encouraged by the fact of its popularity on the Continent, and its nearly universal adoption by the German high-schools. Now that the second German edition has appeared, considerably altered from the first, as well as enlarged, he no longer hesitates in bringing it before the profession of this country. As the authors state in the preface to the first edition, this book is not intended for the physiological chemist, nor for him who is going to make animal chemistry a specialty; neither does it supply the place of many larger works, such as exist in the English language. Every test, every method, is brought home to the student and physician for use in practice. A great amount of space and time is spent upon methods, showing how an examination of urine and diagnosis of disease can be most readily and quickly made. The book, in every respect, is fully up to the times, for which the names of the authors alone are sufficient guarantee.

PREFACE.

The office of the translator has been not only to translate, but, also, in several places, to make slight additions or omissions, being guided therein by his experience as teacher of urinalysis in the Medical College of Ohio. In addition, he has supplied the illustrations, that have been drawn by his student, Mr. W. S. Christopher, and which, he hopes, will make the book more attractive as well as more instructive than it would have been in the German form.

"May the endeavors to increase the utility of this work not be without result."

F. F.

PREFACE TO THE SECOND EDITION.

Comparison with the first edition of this work will show that very many changes have been made. The greater part of the translation has been entirely rewritten. The plates have all been retained, not because of their artistic merit, but because they have seemed to me to show what was wanted in order to bring out certain points. The index is entirely new, and has been written for the special purpose of making the book one that can be easily referred to. The flattering reception of the first edition, faulty as it was, leads me to believe that this, the second, with more notes and in its new form, will take that rank which the original deserves.

F. FORCHHEIMER, M. D.

INTRODUCTION.

The complicated processes which go to make up the basis of organic life result on the one hand, in the building up of the body, and on the other, in changes which have been collectively termed "retrograde metamorphosis," an elimination of effete substances (which can no longer be utilized by the economy); either by the skin and lungs, principally in the form of gas; or by the intestinal tract and kidneys, in the form of solids, or in solution.

To obtain a correct conception of normal or abnormal nutrition, examination must be made into the functional activity of these organs, as well as its results, their excrementitious matter. In the healthy condition of the organism this is exceedingly difficult; in disease of any significance, it is simply impossible. The physician is compelled to restrict his studies, therefore, to one of these excretions—the urine—the most important, fortunately, since by means of qualitative and quantitative changes, it registers, at least approximately, the variations in the life of tissues.

Examination of the urine offers this additional advantage, the fluid can be collected without difficulty, and its analysis, so far as it interests the practicing physician, can be carried out by very simple means.

Not being a lifeless filtering apparatus, the kidney is subjected to disease, to pathological changes, and as a result, substances are mixed with the urine, whose presence alone will lead the physician to a diagnosis of the disease. The urine, then, gives us an insight into the condition, not only of the urinary apparatus, but of the whole body.

On account of the fact that many substances have the peculiar faculty of leaving the system by means of the kidneys, it may be casually stated here that the urine is of great importance to the pharmacologist, and, in some instances, to the medico-legal expert as well as to the physician.

The desire to recognize disease from the appearance of the urine dates from the most remote past of scientific medicine. In his precise and objective observation of the sick, Hippocrates did not disregard its changes.

He instructed his pupils, in accordance with the condition of other sciences, in the semiotic and the prognostic importance of these changes. He demonstrated the physical properties of urine; its quantity, color, and clearness, its cloudy or turbid appearance, and the apparent differences in its sediments, referring these to diseases of the urinary apparatus. Whilst his explanations for these appearances may be very unreasonable, his observations were in the main correct, and led him to conceive the influence of food and drink upon the condition of the urine, which he endeavored to show.

In the post-hippocratic descriptions of disease, we

find the condition of the urine taken into consideration, but the followers of the great Coic physician added nothing to his views. Galen developed these teachings, and systematized them, after which their infallibility was not questioned. But for a long time, no progress was made in this direction, and throughout the following centuries we scarcely find one author, who, through personal observations, has added to these transmitted treasures.

To the Arabian, Iben Sina — 980–1037, — usually called Avicenna, belongs the credit of having pointed out the fact that external causes (such as fasting, vigils, physical and mental exertions) influence the condition of the urine. It was he also, who demonstrated that drugs, taken internally, may cause its temporary discoloration. Beyond this, Arabic physicians did nothing of importance on this subject, notwithstanding the presence of an uroscopist at every oriental court.

In ancient times, and during the middle ages, certainly no one attained such prominence in this specialty as one Johannes, called Actuarius, who lived in the thirteenth century at the court of Byzantium. Adding his own experience to the work of the Hippocrates-Galen school, Johannes describes the physiological changes in urine most minutely, in the seven books of his work "περὶ οὐρων," which are conspicuous for method and clearness of description. This production, which exhausted the possibilities of the allied sciences as they then existed, and the inadequate methods at their command, remained isolate,

and our division of symptomatology was more and more neglected in the time which followed. That it furnished material for satirical representations in Dutch genre pictures, as well as for many comedies of Moliere and other poets, is sufficient proof of its degeneration.

Up to this time all conceptions of the chemical composition of urine were highly defective, so that external appearances alone could be considered by authors of the age. Real progress could only be expected from an adequate development of chemistry and its methods of examination; with Lorenzo Bellini, of Florence, this progress begins. Bellini evaporated urine, and observed that as he again added water, the solids dissolved, returning gradually, step by step, through various intensities of taste and color, almost to the original condition. From this he concluded that the different color and taste of urine depended upon the relation the solid constituents bore to the water, a conclusion upon which, even now, Vogel's scale of colors is based.

Many important chemical discoveries followed soon after this. Willis discovered sugar in urine; Brandt, phosphorus, which, Markgraff stated, came from the phosphates that were contained in the urine.

Rouelle, the younger, discovered urea in 1773, and found that calcium carbonate was present in the urine of herbivora, as well as a substance similar to the flowers of benzoe (hippuric acid). In 1770, Cotugno found albumin in urine; in 1798, Cruikshank connected this discovery with dropsy, and, in 1807, Bright

finally demonstrated the connection between diseased kidneys and albuminuria.

At the same time, chemical analysis of gravel and calculi were undertaken. Among the many publications of merit on this subject, those of Scheele, Wollaston, Wetzlar, and Prout must be especially mentioned.

To two Frenchmen, however, is due the credit of having developed uroscopy to its present position. The researches of Rayer, as shown in his large work, "Les maladies des reins," form the foundation for our present knowledge of kidney diseases.

Becquerel, the son of the celebrated physicist, had for a long time occupied himself with urinalysis, under the direction of Andral, and modestly gives him all the credit of having inspired him with the thoughts for his observations. These observations having extended through many years, he finally published them in the work "Semiotique des urines." For the thirty years following the appearance of this book, many students have devoted themselves to the same branch, so that probably no other division of zoochemistry has so extensive a literature as this.

After this short sketch of the development of our subject, there remains only a brief discussion of the divisions that have been thought necessary for this book.

After a chapter on the microscopic structure and function of the urinary organs, [without a knowledge of which, comprehension of disease is an impossibility,] the physical character and chemical constituents of

urine, *as far as they seem to us important to the practising physician,* are treated of. Upon this follows a description of the microscopical part, *i. e.*, the sediments.

Reviews will be of advantage to the beginner, for whom this little work is intended. The short key to the method of examination he will also find of value. Finally, a description of the simple (uncomplicated) diseases of the urinary organs will be found, in so far as they give signs that can be utilized for diagnosis.

CHAPTER I.

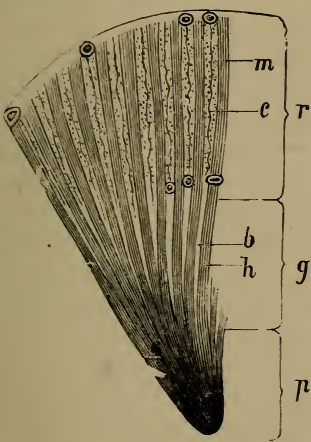
HISTOLOGY OF THE URINARY APPARATUS.

I. The Kidney.*

If a kidney be cut from the papillæ to the fibrous capsules, two concentric layers will become distinctly visible to the naked eye; the central, striped medulla, and the peripheral, more granulated cortex. If the blood-vessels and uriniferous tubules be injected with different coloring matters, other divisions may be seen.

Fig 1.

A longitudinal section of the kidney of a dog; blood-vessels and uriniferous tubules injected.



p, Papillary portion, and *g*, boundary zone of the medulla; the dark rays, *h*, are bundles of uriniferous tubules, which are continued, *m*, into the cortex, and the unshaded divisions of the medullary layer, *b*, correspond to the bundles of blood-vessels of the boundary zone. *r*, Is the cortex, or cortical layer; *m*, the continuation of the uriniferous tubules of the medullary layer, and *c*, the unshaded part of the cortex occupied by dots (glomeruli), represents the labyrinth (after Ludwig).

*The investigations of Kölliker, Schweigger-Seidel and Ludwig were taken as a basis for this description of histological relations.

In the papilla, and in the neighborhood above it, the kidney seems to be uniformly radiate, colored only by the mass injected into the urinary tubes; this division is called the papillary zone of the medulla. Above this there is a section which is also radiate, but beginning to show the mass injected into the blood-vessels. There can here be seen alternate layers of the injected masses. This part is called the boundary zone of the medulla. The third, outer layer, finally, which encloses the others, is known as the cortical layer, and it shows narrow stripes of the two injected colors, in alternate arrangement. Those colored by the mass injected into the uriniferous tubes are the direct continuations of the fibres of the medulla, and are called medullary rays. To the others (showing granules principally, seemingly colored by the mass injected into the blood-vessels), has been given the name of labyrinth, or cortical layer in the strict sense.

Accordingly, we find through the misroscope that the papillary layer is made up chiefly of straight uriniferous tubules; the boundary zone, of these and blood vessels; the pyramids, principally of the straight uriniferous tubules, and the labyrinth, of convoluted tubules, and of convoluted and tortuous blood-vessels.

This system of blood-vessels and uriniferous tubules is supported by connective tissue, which forms a very sparse stroma. It consists of a fine network of connective tissue corpuscles, and is better marked in the medullary layer than in the cortical. Upon the surface of the kidneys the stroma is condensed into a delicate membrane, which is only loosely connected with an

outer fibrous, investing membrane, surrounding the whole kidney, and attached at the hilus to its vessels and the pelvis. This investing membrane is made up of ordinary connective tissue, with a dense, fine, elastic network.

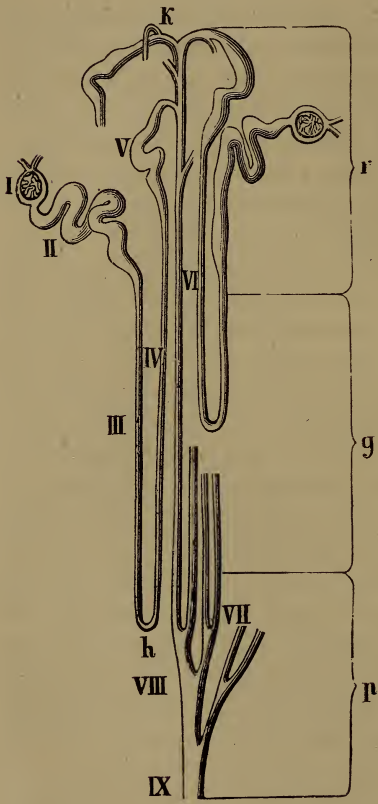
The Uriniferous Tubule originates in the labyrinth, in the form of a spherical dilatation (Capsula Malpighii).* "Then, through a contraction (the *neck of the capsule*) it progresses in the form of a dilated tube, which takes its course in manifold curves toward the medullary portion. When this large convoluted tube reaches the boundary zone, it contracts and penetrates more or less deeply, as a straight narrow canal (*descending, or closed limb of the loop*) into the medullary substance, turns back, making a narrow loop (*Henle's loop*), and runs directly upward, towards and into the cortical substance (*ascending, or open limb of the loop*)."* "Upon returning to the cortex, the tubule, instead of seeking the exact place from which it came, seems to avoid the labyrinth and creeps close to the nearest bundle of medullary rays. Sooner or later, however, it abandons its straight course, enters the labyrinth, as the so-called *intermediate portion*, and proceeds, in more or less angular curves, between the tortuous canals. Soon it turns again, forming an arch whose convexity is directed towards the convexity of the kidney, towards the medullary rays, there to abandon its individual existence in a union with several other converging tubules into one larger and straight tube (*collecting tubule*)."

*This quotation is taken from the classic description of C. Ludwig. (Handbook of Histology, Stricker.)

Such a collecting tubule holds a straight course until it reaches the papillary portion of the kidney, where it unites dichotomously, from time to time, with neighboring collecting tubules, until finally it empties itself (*ductus papillaris*) upon the surface of the papilla.

Fig 2.

Schematic representation of the course of a uriniferous tube; human kidney.



p, Papillary layer; *g*, boundary zone of the medulla; *r*, cortical substance (I), capsule of glomerulus, which enters into tortuous portion (II), through its neck. The tortuous portion contracts at the boundary between medulla and cortical, into (III) the descending limb of the loop, and as such, goes through (*h*) Henle's loop, into (IV), the ascending limb of the loop. To this is added (V), the intermediate portion, which through (*r*) the external loop at the top, enters the collecting tubule. The collecting tubule unites with (VII) its neighbor of the same medullary

ray to form (VIII) the principal tube, and this in turn unites with others until it finally forms (IX) the ductus papillaris.

The walls of the Malpighian capsule are made up of mosaic cells, like those of blood and lymph capillaries. The external surface, or tuft, of the glomerlus is covered by a layer of cells, containing spherical nuclei, and not distinctly separated from each other, which prevent its being washed directly by the fluid contents of the capsule.

"From the neck of the capsule to the commencement of the papillary duct, the wall of the tubule is composed of a tunica propria, and a layer of epithelium resting upon its inner surface." The tunica propria is homogeneous, transparent and elastic. The epithelium, which invests the inner surface, consists of one layer, which is possessed of nuclei, whose form is everywhere the same; spherical and sharply defined, and whose contents show many granules. The body of the cell, on the contrary, varies largely in shape. In the arched, tortuous tubules the epithelium forms a collected, gelatinous, cloudy mass, in which nuclei are imbedded at equal distances from each other; a division into cells corresponding to these nuclei, seems to be entirely absent.

"This epithelial pulp sits very loosely upon the basal membrane," and the whole substance can be easily forced out of the cut tubules in the form of a cylindrical mass. With the microscope, this is found to contain many oil globules, as well as other dark corpuscles (cloudy swelling of the epithelium), which, upon the addition of dilute acid, are cleared up; but,

after being thus cleared, it is often impossible to distinguish anything, except the nuclei of the cells in the mass.

In the small tubules, which form the limbs of the loop of Henle, there appears, instead of the dark and bulky epithelium already described, a light and meager one, covering the walls of the tubule, with a continuous layer of cells, which are much bulged out by the nuclei.

Beyond Henle's loop, where the diameter of the tube increases, the epithelium appears to consist entirely of cylindrical cells, arranged like the shingles of a house, the one above the other, and following the direction of the tube, from the medullary to the cortical layer.

The gelatinous layer, which is common to the tortuous canals, is again found in the intermediate portion.

In the collecting tubules, including the papillary duct, the epithelium is composed of distinctly separated cylindrical cells, with their bases upon the tunica propria, and their blunted points toward the lumen of the tube.*

*[R. Heidenhain (Handbuch der Physiologie. Hermann, Bd. V. p. 284–288), who, for over ten years, has been able to distinguish differential markings in cells, describes the lining of the uriniferous tubules, as follows:

In the tortuous canals he finds epithelial cells of a peculiar character; their protoplasm consists of fibrils or rods agglutinated by unchanged protoplasm. They form a broadened base, which rests upon the membrana propria, and towards the lumen of the tubule they end in undifferentiated protoplasm which surrounds the cell nucleus. This undifferentiated protoplasm is continuous with that forming the cement substance of the rods. Some of the rods seem to pass the unclear zone, but they never reach the lumen of the canal. In the *descending limb of Henle's loop*, the epithelium consists of very flat spindle-shaped cells, with badly-defined outlines, whose nuclei project far into the lumen of the canal. *In the ascending limb* of the

Blood-Vessels of the Kidney.—The renal artery sends the greater part of its blood through the cortical portion. Its branches penetrate to the boundary of the cortex without forming a network, and then rapidly divide into very minute arteries; the arteriolæ interlobularis and arteriolæ rectæ. The interlobular arteries run between two medullary rays, i. e., where several primitive bundles are found together. Arrived in the layer of tortuous tubules, they give off a branch to each Malpighian capsule. This branch (Vas afferens glomeruli) perforates the spherical end of the tubule (or, according to other authorities, pushes the same before it), and here terminates "in a pendulous bundle of capillaries (glomeruli), which in their turn, are collected within the capsule, into one venous branch (Vas efferens glomeruli)."

This venous radical comes out of the capsule at the place where the artery enters it. After leaving the capsule "it proceeds toward its medullary ray; or,

loop the epithelium is the same as in the tortuous canals, differing only in the length, both absolute and compared to the size of the cells, of the rods. In the intermediary portions that have the same diameters as the tubuli contorti, are found highly refractive cylindrical cells, with large nuclei and a small amount of protoplasm. Where the cell rests upon the tunica propria the protoplasm spreads, so as to form processes which lie upon processes coming from neighboring cells. In intermediate tubes of smaller diameter the epithelium is lower. In the collecting tubule, within the medullary ray, are found cells approaching the cylindrical in type, but presenting the same peculiarities as described in connection with those of the intermediate portions of large diameters. As we descend, we find typical columnar epithelium, becoming higher the nearer we approach the papillary duct. Heidenhain divides the uriniferous tubule into two portions—the secretory and the efferent. The secretory portion consists of those parts included between the Malpighian tuft and the beginning of the medullary; the efferent, those between the beginning of the medullary ray and the opening of the ductus papillaris."]

where this is lacking (as in the outermost layer of the cortical substance), directly to the tortuous tubules, and splits up into a number of capillaries, which immediately combine to form a network," thus producing meshes which surround the uriniferous tubules. All the efferent vessels communicate with each other by means of their capillaries, forming a continuous capillary network, which occupies the whole cortical substance; this, in its turn, anastomoses with the meshes around the pyramids, and a connection is thus established between the capillaries of the medullary and cortical portions.

Venous trunks are formed by these capillary nets. In that part of the cortical in which no glomeruli are found, the veins originate in the form of stars (Venæ stellatæ). The common trunk penetrates that part of the cortex which is supplied with tufts and tubules, seeks the neighborhood of an interlobular artery, where it takes up many veins from the surrounding cortical portion.

The veins of the medulla (venulæ rectæ)' run in those spaces which are occupied by the arteries, and unite at the border of the cortex, with the veins coming from the latter, to form large trunks.

The capsule of the kidney receives its blood-vessels partially from the interlobular arteries, and partially from other neighboring trunks (the phrenic, lumbar and supra-renal arteries). Some of their capillaries enter the stellate veins; some enter veins corresponding to the arteries that have supplied the blood.

The *Nerves* of the kidney are derived from the

coeliac plexus of the sympathetic. They follow the course of the larger vessels, as well as the lymphatics that enter the lumbar glands. Their final terminations are not known.

II. Efferent Passages.

The *Ureters*, *Pelvis of the Kidney* and the *Calyces* are made up of an external fibrous membrane, a layer of unstriped muscular tissue, and a mucous membrane. The fibrous coat is continuous with the albuginea of the kidney, and consists of connective tissue and elastic fibres. In the ureters, the muscular layer is made up distinctly of three divisions: the inner one runs longitudinally, the middle one transversely, and the outer, which is the thinnest, again longitudinally. In the pelvis the relations are the same, except that in the calyces the muscular layers become thinner and finally disappear where they touch the papillæ. The mucous membrane is thin, rather rich in blood-vessels, without glands or papillæ. The epithelium is present in layers, and is characterized by the varied form and size of its elements. In its deep layers, the cells are round and small; in the middle layers, cylindrical or spherical, with prolongations; and at the surface, rounded, many cornered, or frequently flattened, and of larger size.

The *Bladder* possesses the same membrane as the ureters. The muscular layer is frequently quite thick, but the individual fibres are distributed so irregularly that their schematic course cannot be described. Internally there is usually found a net of circular bun-

dles which cross each other at acute angles, thus forming meshes which lie transversely. These circular fibres are thickest at the opening of the bladder, and there form its sphincter. Upon these circular bundles, follow longitudinal fibres which are of inconstant distribution. The trigonum consists simply of a thickening of the connective tissue layer, extending from the opening of the ureter to the caput gallinaginis. The mucous membrane (except at the trigonum), especially at the neck and fundus of the bladder, has a thick sub-mucous layer, which is rich in blood-vessels and nerves.

At the neck of the bladder, and towards the fundus, are found simple racemose glands, having cylindrical epithelium and mucous contents.

In the bladder the epithelium is found arranged in several layers. Innermost are found cells of a decidedly flattened form, but differing largely both as to size and shape, the one from the other. The middle layer is usually composed of young conical cells, with their apices toward the cavity of the bladder, and whose processes can be frequently traced into the deeper layer. The outer layer is made up of ovoid cells; irregular, and frequently drawn out, where they are in contact with the middle layer.

The superior and inferior vesical arteries (branches of the hypogastric) supply the bladder with blood. They pierce the wall of the bladder at the fundus, pass obliquely through the muscular coat, giving off branches to the same, and then divide into capillaries in the connective tissue under the epithelium.

In the connective tissue at the fundus, nerve fibres are not very numerous, but the medullary sheath can be detected in all of them; their terminal branches are not known. The vessels and nerves of the ureters are analogous to those of the bladder.

The *Male Urethra* has a corpus cavernosum whose structure is like that of the penis, fibrous membrane and meshes, only much more delicate; and a glandular organ—the prostate gland, which forms its support. Under the mucous membrane, throughout its whole extent and below it, there is a well developed connective tissue layer, rich in elastic fibres; there are also to be found here organic muscular fibres, arranged both longitudinally and transversely.

The epithelium of the male urethra is cylindrical and arranged in layers; with the exception of the exterior part of the fossa navicularis, where papillæ and flat epithelium are already to be found. The cells of the accessory glands, those of the prostate, Cowper's and Littre's glands, and of the vesicula prostatica are conical and can hardly be distinguished from those of the urethra.

The *Female Urethra* has no corpus cavernosum; its mucous membrane is rich in vascular supply, and has flat epithelium in layers. In addition there are very few glands of Littre to be found in it.

CHAPTER II.

Secretion of the Urine.

The function of the kidney is to secrete the urine; that of the bladder and ureters, on the other hand, to collect, retain, and carry it off. A theory which is entirely satisfactory, and explains all facts concerning the secretion and excretion of urine, does not, as yet, exist.

Bowman, basing his views upon the anatomical structure of the kidneys, thinks that the epithelial cells are secretory organs, and that water only is excreted by the tufts, which washes the constituents of urine out of the epithelial cells.

Ludwig bases his theory, on the one hand, upon the different amount of blood pressure in the various blood-vessels of the kidney; on the other, upon the different capacity that substances possess of passing through animal membranes. He assumes that the pressure upon the glomeruli is greater than in the capillaries surrounding the uriniferous tubules. As a result, an abundant transudation of water and salts in solution, (serum of blood, little albumin and fat) must take place from the blood into the Malphigian capsule. Thus, very dilute urine is to be found in the uriniferous tubules, and highly concentrated blood, in the capillaries surrounding the tubule.

These two fluids, differing so widely in density, and separated from each other by animal membrane, produce active currents of diffusion; as a result, water is added to the concentrated blood, on the one side, and on the other, products of retrograde metamorphosis (urea) and salts, are added to the dilute urine in the uriniferous tubules. In this way the watery urine becomes more concentrated, richer in urea and salts; becomes urine. The absence of albumin is to be explained, in that this substance does not easily pass through animal membranes, and then only as a result of increased pressure (the walls of the blood-vessels and tubules are animal membrane); accompanying pathological conditions, with increased pressure in the glomeruli (stasis in the veins of the kidney) albumin is always found in the urine, but under normal pressure this is never the case. Although this theory explains many physiological and pathological facts, yet it does not explain how an alkaline serum of the blood produces an acid urine. According to this mechanical theory of Ludwig, the secretion of urine is a process of filtration taking place in the glomerulus and a process of diffusion throughout the course of the tubules; the epithelial cells lining the tubules are not taken into consideration at all.

According to Goll and Max Hermann, the difference in pressure between the contents of the vessels and urinary tubules, is the principal force that causes the transmission of the constituents of the urine from the blood to the tubules. According to this, when pressure is increased in the renal artery the quantity of

urine immediately increases; but when the pressure in the artery is diminished, or when pressure in the ureters is increased, blood pressure remaining normal, secretion diminishes, and may cease entirely, long before the pressure in the ureters equals that in the renal artery.

Ustimowitsch and Grützner have elaborated this theory, in so far that they showed by experiments on dogs, that the local pressure in the glomeruli only, not the general blood pressure, must be taken into consideration.

Upon section of the medulla in a dog, and electric irritation of the same producing increased blood pressure, secretion of urine ceased entirely, because the smaller vessels of the kidney contracted. If, in addition, the nerves going to one of the kidneys were divided, there would follow on that side a profuse flow of urine, whilst on the other no urine would flow from the ureter. By means of division of the nerves going to the kidneys, its smallest arteries become dilated and relaxed, thus increasing pressure in the smaller vessels and stimulating the flow of urine.

In addition, Ustimowitsch demonstrated that an increase in secretion of urine can take place, even when the general blood pressure is diminished. If the splanchnic nerve (which contains the vasomotoric tracts for the kidney) be divided, the pressure in the aorta is diminished; at the same time, however, dilatation of the smaller arteries in the kidney ensues, so that an increase in secretion can be verified.

Heidenhain and Wittich support Bowman's views

concerning the secretive function of the epithelium in the tortuous uriniferous tubules, for they show by experiments with indigo sodium sulphate, sodium urate and ammonium carminate, that these substances are principally secreted by this epithelium.

According to the experiments of K. Muller, the quantity of urine is increased by the action of cold upon the skin; and is decreased by warm baths, or varnishing the surface of the body, the latter producing dilation of the blood-vessels in the skin.

An increase in the circulation of the skin, then, increases; a diminution of the same, decreases, the secretion of urine.

Maly, Donath and Posch claim that an aqueous solution of various salts, having a neutral or even an alkaline reaction (mono and di-sodium phosphate), may, when subjected to osmosis, produce a solution of acid reaction. This is exceedingly important, because it obviates the necessity of ascribing to the epithelial cells the property of causing the formation of acid.

As all the physiological and chemical processes which take place during the secretion of urine are not completely explained by the hypotheses thus far brought forward, we must still look upon this process as a combination of secretion and filtration.

CHAPTER III.

THE URINE.

A.—In General.

Urine is the secretion of the kidney, and in the normal condition, represents, in the main, a solution of the substances which result from retrograde metamorphosis.

It is a solution of urea and common salt, to which are added, in small quantities, other organic and inorganic constituents of the blood; also, certain substances introduced into the system, which are excreted, either in their unchanged condition, or after having undergone a chemical decomposition.

Normal urine contains as organic constituents; urea, uric acid, creatinin, hippuric acid, xanthin, lactic acid, grape sugar (Brücke), etc.; inorganic constituents; sodium chloride, sodium, calcium, and magnesium phosphate, sulphates of the alkalis, ammonium, and iron salts, combined with coloring matter and gases; carbon di oxide, nitrogen and oxygen.

In pathological urine there can be detected, in addition to these normal substances, albumin, grape sugar, inosit, constituents of bile, fats, hydrogen bisulphide, blood coloring matter, uroërythrin (Heller), leucin and tyrosin, calcium carbonate and oxalate, ammonium carbonate, cystin, pus, blood, epithelial structures, spermatoza, fungi and infusoria.

Before considering the symptomatological value of urine, we must look at its properties(as far as they interest us), and the most valuable methods for its examination.

B.—Physical Properties.

I. Quantity.

The quantity of urine voided by a healthy man, eating and drinking in moderation, during twenty-four hours. varies from 1400–1600 c. c.; average, 1500 c. c.

The greatest quantity is secreted during the afternoon; the smallest, during the night; the mean occurs in the morning, and, at this time, the urine represents in every respect, an average, being least influenced by meals.

By means of the introduction of fluid into the system, the quantity of urine can be enormously increased (urina potus); an increase, less marked, can be noticed during very cold or moist weather (less perspiration). During rest or profuse sweating, and copious diarrhœa, the quantity is diminished.

II. Specific Gravity.

The *Specific Gravity* of normal urine of 1.500 c. c. quantity is from 1.015 to 1.021. If the quantity increases or diminishes the specific gravity changes in inverse ratio. In pathological cases the specific gravity varies from 1.003 to 1.040. Those cases are of special

importance, in which, with small volume, there is low specific gravity, or with great volume high specific gravity. A high specific gravity is found frequently in diabetes mellitus, in the beginning of acute diseases and during the administration of salts. Urine great in quantity, having a specific gravity of between 1.003 and 1.040 is always very suspicious as indicating diabetes mellitus. A low specific gravity is observed in hydruria, urina spastica and urina potus.

Specific gravity can be accurately determined, either by means of the picnometer or the scales of Westphal. For practical purposes, however, small areometers (called urinometers) are employed.

When specific gravity is to be determined by means of the urinometer, a suitable vessel is filled four-fifths full, all air-bubbles are removed with filtering-paper, and the urinometer then introduced in such a way, it is allowed to slide between the index and middle finger of the right hand. The urinometer must not be allowed to touch the walls of the vessel. Bring the eye on the same plane with the surface of the fluid, and read from that division of the scale which corresponds with the surface of the urine (not with that surface which is drawn up on the scale by means of attraction).

[Note.—A simple rule is to read from the lowest level of the fluid; in this way both attraction of the walls of the vessel, and also of the stem of the urinometer, are disregarded.]

Then the urinometer is immersed into the fluid and again read.

In taking specific gravity with the urinometer, the temperature must be between 12–17° C., otherwise a great error may arise.

If the quantity of urine for observation be very small, it is to be diluted with two, three or four times its volume of water, the urinometer is then introduced, and the result is multiplied by the diluted volumes. Thus, if one volume of urine has been diluted with three volumes of water, and the areometer marks 1.008, the real specific gravity is obtained from this apparent specific gravity by multiplying the last two figures of 1.008 by $1 + 3 = 4$:

$$1.008 \times 4 = 1.032.$$

The same quantity of solids which was dissolved in one volume before, is now dissolved in four; the specific gravity, after dilution, is, therefore, only one-fourth of the real, or the real specific gravity is four times that of the dilute.

III. Solids.

The quantity of solids excreted by the urine in twenty-four hours varies from 60 to 70 grammes. If a greater amount than 200.00 gr. is found, we are dealing with DIABETES. If, on the other hand, the quantity being nearly normal, we find 21.00 grammes only, we have HYDRURIA. In order to determine, approximately, the quantity of solids present in twenty-four hours, either Trapp's (2) or Haeser's (2.23) co-efficient may be employed. (For accurate determination, see

Chapter V.) First, the specific gravity of the urine is found. The last two figures of this are multiplied by the co-efficient, and the product is the quantity of solid constituents found in 1000 c. c. (in grammes). The quantity of urine being known, it is easy to determine how much is found in twenty-four hours. For instance, given a urine of 1500 c. c. in quantity during twenty-four hours, its specific gravity 1.020; in order to find the amount of solids in 1000 c. c., the last two figures (20) are multiplied by Haeser's co-efficient, 2.33:

$$20 \times 2.33 = 46.60.$$

This product represents the amount of solids, in grammes, in 1000 c. c. of urine; from this the proportion:

$$1,000 : 1500 :: 46.60 : x,$$

is readily established, and its solution, $x = 69.90$ is the quantity in twenty-four hours; nearly the normal quantity.

In the following, the quantity of solids in twenty-four hours in various specimens of urine will be given:

Ex. I.—Quantity, 4,000, c. c.
Sp. gr. 1.007.
$07 \times 2.33 = 16.31.$

1,000 c. c. urine, therefore, contain 16.31 grains solids—4,000 c. c. = 65.24 gr. From this we see that the quantity of solids is normal, that the water alone is increased.

Ex. II.—Quantity, 6,000 c. c.
Sp. gr. 1.013.
$13. \times 2.33 = 30.29.$

In 1,000 c. c. urine we have 30.29 gr. solids in 6,000 c. c.

$$1{,}000 : 6.000 :: 30.29 : x$$
$$x = 181.74 \text{ gr.}$$

In this urine the solids in twenty-four hours are more than double the normal quantity, showing a case corresponding in this respect to that of diabetes.

Ex. III.—Quantity, 2,000 c. c.
Sp. gr. 1.005.
$05 \times 2.33 = 11.65$ gr.

1,000 c. c. contain $11.65 - 2{,}000 = 23.30$ gr. The solid constituents are very much diminished—an hydruria.

The differential diagnosis between diabetes insipidus and hydruria on the one hand, and urina potus on the other, and also between oliguria and normal urine, can be made simply by taking the solid constituents of the twenty-four hours into consideration.

Other important deductions can also be drawn from the quantity of solids and the specific gravity, the observer being led to these by each individual case. Thus, where a disease of the kidney is proven, the quantity of urine being normal or diminished, and the specific gravity being very low, the deduction can be drawn that as urea represents nearly one-half the solids, this substance is not excreted in sufficient quantity, and uræmia may be imminent, etc.

On account of the fact that the relations of the dissolved fluids to each other is not a fixed one, computation from specific gravity cannot be accurate. An error of 6% can be made (in abnormal urine even more), *i. e.* having computed in 1,000 parts 50 gr. of solids, and finding only 47 or 53 gr. on the next day,

we cannot say that the solids have increased or diminished.

In judging the changes in the body by the specific gravity, we must, in addition, take into consideration whether or not the usual amount of food is taken up, or (as in acute diseases) whether the patient abstains from food. In the latter instance, an average of 30.00 gr. must be taken, so that the patient passing 40.00 gr., having pneumonia and abstaining from food, really passes more than the normal quantity—an increase that takes place at the cost of the body.

IV. Consistency.

The consistency of normal urine is that of a thin fluid, easily to be separated into drops. Under pathological conditions it sometimes becomes thick. When a great amount of pus is present in alkaline urine, the urine can be drawn out like the contents of a cyst containing paralbumin: diluted with water and precipitated with acetic acid, a dense cloudiness arises, which is an alkali albuminate, formed by the action of the alkaline urine on pus.

In Isle de France, it is stated that urine is seen which coagulates in the vessel like lymph, and contains fibrin (fibrinuria). In our zone this form of urine is exceedingly rare. In several cases of papillary tumors of the bladder we have observed temporary fibrinuria.

Urine, fluid at the time it was voided, reddish-yellow and containing very little blood, a few minutes

afterwards was changed to a trembling, gelatinous mass, which could no longer be poured from the vessel containing it.

Upon shaking normal urine, foam is formed which disappears in a very short time when the vessel is put down; if the urine contains sugar or albumin the foam will remain for some time. (Bile also gives to urine a certain amount of tenacity, so that bubbles are retained upon the surface for some time.)

V. Color.

The normal color of urine of 1.020 sp. gr. and 1,500 c. c. quantity in twenty-four hours is wine-yellow. In concentrated urine it varies from dark wine-yellow to that of amber; in diluted, from pale wine-yellow to straw-colored. The urine passed in the morning, or when people have perspired, always has a dark color, but in urina potus it is light. In addition, in pathological conditions, the urine undergoes much greater changes, for which, very commonly, abnormal coloring matter must be looked upon as the cause.

Urine can be divided into the following varieties, in respect to color:

1. *Nearly Colorless.*—In neuroses, especially, do we meet with a "urina spastica," which can hardly be distinguished from water. In other varieties of hydruria and in diabetes the coloring may be very faint, although yellow is unmistakable. A change, however, can set in in the course of a few hours, so that then darker urine is passed.

Light urine arises from the presence of the normal quantity of coloring matter in much water (urina potus, urina spastica) or normal amount of water and diminished coloring matter (as in the granular kidney); in most cases both factors are present.

2. *Highly Colored.*—Dark yellow, somewhat reddish, to red. This color is not only produced by concentration, but frequently by the presence of uroërythrin. It is met with in febrile conditions, in the stages of increase and acme.

3. *Blood Red to Garnet* is always produced by the presence of some foreign coloring matter. Numerous substances from the vegetable kingdom, when excreted by the kidneys impart to alkaline urine a red color. The same occurs when blood is found in the urine.

4. *Dark Brown to Black* is caused by the presence of methæmoglobin in diseases of the kidney, especially hemorrhages; by the presence of biliary coloring matter in the urine (icteric urine-jaundice) and by coloring matter not definitely known; as in long continued attacks of intermittent fever.

Sometimes in melanotic cancers, after the urine has been allowed to stand for a long time, it becomes black. As this form of coloring matter has been found without the presence of a cancer, and *vice versa*, not much symptomatic reliance can be placed upon its presence or absence. After the external use of carbolic acid (for example, when Lister's method is employed) very dark urine is also observed, but this is not constant.

Occasionally in the urine of children, a brownish

discoloration going from the surface to the bottom is observed, due to the presence of pyrocatechin. In lepra, as the fatal end approaches, we see the dark red urine changed to a dark brown (urorubrohematin).

5. *Green*, of a dirty shade, is produced in jaundice by the presence of biliverdin, and is of the same importance as brown icteric urine.

6. *Bluish*, producing a dark blue film and a similar precipitate of indican. This urine is always alkaline—most frequently met with in cholera and typhus.

VI. Transparency and Fluorescence.

Normal urine is always clear and transparent, and only after it has stood a long time can we distinguish a small cloudiness of mucus (nubecula). With the microscope this is found to contain round and flat epithelial cells.

The nubecula is usually more abundant in females, and more epithelium is found in it, especially in layers, coming from the genitals.

Pathologically the urine becomes cloudy from all the substances that are found in the sediment. To detect the chemical nature of the turbidity, the following method is employed: A test-tube is filled one-third full of the urine to be examined, and carefully heated over the lamp.

(*a*) If the cloudiness disappears entirely, urates which are beginning to be precipitated are suspended.

(*b*) If the cloudiness does not disappear, but rather seems to increase, it may depend on carbonate of cal-

cium, the earthy phosphates or albuminous cellular elements (pus, blood). For differentiation a few drops of acetic acid are added.

If the urine clears up, the earthy phosphates have caused the turbidity; if not, or if the turbidity increases, suspended pus or blood can in most cases be considered as the cause. Albumin also causes the latter reaction.

(*c*) If the urine does not undergo any change when heated, and a slight increase in cloudiness, only, be detected, an abnormally great amount of mucus and bacteria can be deduced.

There is sometimes a marked fluorescence in normal urine; as yet we are unable to state the substances that produce it.

Alkaline urine appears greenish by reflected light; by transmitted light, yellowish red. Some urine shows the spectrum of urobilin.

VII. Odor.

The odor of fresh human urine is faintly aromatic. The substances causing this are unknown. If the urine has undergone alkaline fermentation, a distinct ammoniacal odor is perceptible. In destructive processes in the bladder, a peculiar, fetid, sometimes fecal smell is present. Upon the introduction of certain articles of food, or the taking of certain drugs, the odor of the urine is changed in a marked manner; for instance, after eating asparagus, cauliflower, etc. After

turpentine, the odor is like that of violets. The odoriferous principles of cubebs, saffron, etc., can also be detected in the urine.

VIII. Reaction.

Normal urine has an acid reaction; this depends principally on the acid phosphate of the alkalies. It may depend, also, upon free organic acids (lactic?). At all events, the role played by these acids in producing the reaction is secondary.

If to a fluid containing free acid, a solution of sodium hyposulphite be added, it becomes turbid on account of the precipitation of sulphur. If this experiment be tried with urine, even after it has stood twenty-four hours, a very slight turbidity sets in, or sometimes, none at all; therefore (even if we do not consider this test as absolute), the amount of free acid in the urine cannot be very great.

After a meal, alkaline urine is sometimes voided; this, however, disappears in a short time, and is of no clinical importance.

Great acidity of the urine is important to the physician, in that it may favor the development of sediments or concretions, and may give rise to irritation of the kidneys and urinary passages (Vogel).

Acid reaction may be changed to neutral or even alkaline. The internal administration of carbonates of the alkalies and earths, or organic salts (acetates, pomates, tartrates), which change to carbonates in the organism, may cause the urine to become alkaline.

The urine may also be alkaline from ammonium-carbonate, being formed by urea having taken up water. At first, the quantity of ammonium-carbonate is only sufficient to neutralize the urine; neutral reaction would, therefore, possess the same importance as alkaline.

Urine of strong alkaline reaction always justifies the conclusion that the bladder is diseased, provided excretion of carbonates of the alkalies has been excluded. The test usually employed is very delicate bluish violet, and faintly red litmus paper.

We must discriminate between the change to alkaline taking place before or after the urine has left the bladder. Furthermore, whether the alkalinity depends upon ammonium-carbonate (splitting up of urea), or fixed carbonate (absorption). This can be done by allowing the litmus paper to lie in a warm place until it becomes dry; if ammonium has produced the change, the red color reappears; if this does not take place, the alkalies present are fixed.

Occasionally urine is observed that turns blue litmus red, and red, blue. This reaction is known as the *amphoteric*, has found no explanation, and has no symptomatic importance.

CHEMICAL COMPOSITION.

(a) NORMAL ORGANIC CONSTITUENTS.

We preface the discussion of the individual substances by a table representing the average quantity excreted. In twenty-four hours there are voided:

	Grammes.	Per cent.
Solids	60—70	4.3 —4.6
Urea	30—40	2.5 —3.2
Uric Acid	0.4 — 0.8	0.03 —0.05
Creatinin	0.5 — 1.0	0.036—0.062
Hippuric Acid	0.3 — 1.0	0.02 —0.06
Chlorides	10—13	0.7 —0.8
Earthy Phosphates	0.9 — 1.3	0.07 —0.08
Phosphoric Acid	2.5 — 3.5	0.19 —0.22
Sulphuric Acid	1.5 — 2.25	0.16 —0.17

From this we see that the greatest amounts are represented by urea and the cholrides. It is easily understood, also, how the absence or insufficient presence of one of these substances would produce a marked effect upon the specific gravity. This does not hold good, to the same extent, for the other normal constituents, as they are excreted in relatively very small quantities.

The amount of gases is practically unimportant. Carbonic acid gas is present in greatest amount (60—150 c. c. in 1000 c. c. urine). Nitrogen is present in very small amount, and of oxygen, traces only can be found.

I. Urea.

Urea CH_4N_2O is the most constant constituent, and the one that occurs in greatest amount. In twenty-four hours a healthy adult will excrete between thirty and forty grammes of urea. Animal diet produces a greater quantity of urea than mixed, and the latter, more than vegetable food, exclusively. In inanition the quantity falls to twenty, and even fifteen grammes.

The latter figures must be taken into consideration, if we wish to form an idea of the changes in the economy of patients put upon absolute diet.

The simplest way of obtaining urea from urine is as follows: After precipitating the inorganic salts with the barium solution used in the volumetric urea test, evaporate to dryness, extract with alcohol, filter, then evaporate the alcohol; finally recrystallize with absolute alcohol.

Another method consists in concentrating urine to the consistency of a thin syrup, then adding pure nitric acid (cold); as a result, urea nitrate will be precipitated. These crystals are decomposed with barium carbonate, and after drying, the urea can be extracted by alcohol.

Synthetically, urea can be made from ammonium cyanate; 80 parts of potassium ferro-cyanide are melted in a crucible with 30 parts of potassium carbonate. By means of 150 parts of litharge, the potassium cyanide which has been formed (CNK) is changed to the cyanate CNOK. This is then poured upon an iron plate; when cool it is dissolved in a solution of 80 parts of ammonium sulphate ($(NH_4)_2SO_4$) in 500 parts of water; a double decomposition takes place, producing CN O,H_4N (ammonium cyanate) and K_2SO_4 (potassium sulphate). Filter and dry. During evaporation, the transposition of atoms takes place, so that from ammonium cyanate we obtain urea, as follows:

$$O^{CN}_{NH_4} \quad = \quad CO^{NH_2}_{NH_2}$$

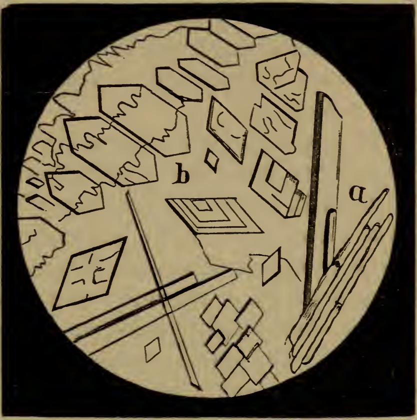
(Ammonium cyanate.) (Urea.)

The dried mass is extracted with alcohol, and allowed to crystallize.

When examined through the microscope, the crystals formed by urea are seen to be glistening white needles; when viewed by the naked eye they seem to be long, transparent, quadrilateral prisms, whose

ends are terminated by one or two slanting planes. It is easily soluble in water and alcohol, but insoluble in ether. Heated moderately on platinum, it melts and develops ammonia. Mixed with putrescent urine, or the secretion from cystitis, it is separated in the opposite direction from its formation. It splits into 1 molecule of carbonic acid gas, and two molecules of ammonium, taking up 1 molecule of water ($CH_4N_2O+H_2O=CO_2+2H_3N$).

Fig. 3.



a, crystals of urea; *b*, crystals of nitrate of urea.

This same decomposition takes place when boiled with strong mineral acids, melted with caustic alkalies, or when heated with barium hydrate in a sealed tube. When nitrous acid, sodium hypochlorite or hypobromite are added, urea is split up into carbonic acid, water and nitrogen.

Urea is carbamide. For details see K. B. Hofman's Zoochemistry—in English—Fowne's Elementary, or Kingzett's Animal Chemistry.

Mercuric nitrate with solutions of urea produces a flaky white precipitate, equaling 2, 3, or 4 equivalents of mercury to 1 of urea, depending on the concentra-

tion of the fluid. Urea also enters into combination with common salt.

When nitric acid is added to concentrated urine, or to a concentrated solution of urea, beautiful rhombic plates are formed, which may frequently be seen with the naked eye.

If one has only a drop of fluid which must be tested for urea, this is put upon a slide, and a drop of nitric acid is added; this is gently heated over a spirit lamp, then put aside to crystallize. Under the microscope there are observed, either single rhombic or hexagonal plates, or these are seen in great number, more or less developed, lying upon each other like shingles, and in rows, generally intersecting each other at right angles. The acute angle of the rhombus is 82 degrees. This test is most frequently resorted to on account of the facility with which it is carried out, and also on account of the characteristic form of the crystal of nitrate of urea.

In albuminuria the nitrate of urea takes another form, that of brush-shape needles. (Hoffman, l. c.)

A concentrated solution of urea, decomposed by oxalic acid, produces crystals that look like those of nitrate of urea; but as this form does not appear so regularly as the former, this reaction is looked upon more as one corroborating and verifying, having been preceded by the nitric acid test.

These reactions can all be carried out with concentrated urine, but when albumin is present, this must first be gotten rid of by means of coagulation.

If the question comes up whether a fluid is urine,

the first thing to be decided upon would be the determination of the presence of urea and uric acid. If a few drops only were presented, the micro-chemical reaction for urea would be decisive. We must not forget, however, that some transudations contain urea.

As urea, of all the constituents of urine, is present in greatest quantity, we can deduct from the specific gravity the approximate quantity of urea, provided no sugar and no great amount of albumin can be detected, and provided the chlorides be present in normal quantity. This being the case, and having a urine whose specific gravity is between 1020 and 1024, we can state that such an urine contains a normal percentage of urea, *i. e.*, between 2 and 2.5%. If, under the same conditions, we find increased or diminished specific gravity, we can state that the percentage of urea is correspondingly increased or diminished. If the specific gravity is 1014 the urine contains about 1% of urea; if 1028—1030, it contains 3% of urea.

If the chlorides are present only in small quantity, or can not be detected at all, as occasionally happens in acute febrile diseases, even with normal specific gravity, then the percentage of urea is increased. For the 16 grammes of chlorides that are present in normal urine, and which form the second greatest factor in influencing specific gravity (always excluding sugar and albumin), are absent in this case, therefore the specific gravity of 1020 must be produced by the urea; for all the remaining constituents of urine, uric acid,

creatinin, the phosphates and sulphates, even if their normal quantity be doubled, could have very little influence upon the specific gravity.

If albumin is present in moderate quantity (0.2%) it has very little influence upon specific gravity, and can be neglected entirely in the approximation of urea; this can be ascertained by means of the nitric acid test, which, in this case, would produce a translucent layer of precipitate. But if albumin be present in greater quantity (1—2%) it must be removed by coagulation, and the filtered urine must be examined after it has cooled off.

For this purpose it is best to take a given quantity of urine, for instance, 50 c. c.; after adding a few drops of acetic acid, heat in a flask to the boiling point; allow it to cool, then filter, and wash the filter paper with distilled water until the fluid lost by evaporation is made up. Thereupon the specific gravity of this urine that has been deprived of albumin, is determined.

Urine containing albumin is usually in and of itself, of a lighter specific gravity than the normal urine. The diseased urine-producing organs can not secrete urine containing the normal quantity of excretory material (especially urea). As a result, the specific gravity must become less. The quantity of albumin is rarely sufficiently great to substitute the urea in regard to specific gravity.

When sugar is present in large quantity the per cent. of urea is always diminished, although the

entire quantity of urea excreted is always increased. The high specific gravity depends upon the sugar.

Notwithstanding many statements to the contrary, we have never succeeded in obtaining urea artificially from protein. Still, this must be considered as its only source.

Urea is not the only measure of tissue change, but it is the most important one. It owes its origin, partly to the retrograde metamorphosis of tissue (including blood), and partly to the decomposition of superfluous nitrogenous food. Whether it originates in gradual oxidation; whether its molecule is separated from one more complex, by means of fermentation; whether this separation takes place from the albumin-molecule directly, or from a gradual division of this molecule into smaller ones (intermediate molecules), from which, by oxidation, urea is generated, is, as yet, undecided. It is proven that certain combinations that are found in the body, belonging to the uric acid group (uric acid, allantoin, creatin, sarcin, xanthin, guanin,) and certain derivates of protein (glycocoll, leucin, aspartic acid,) when introduced in considerable quantities into the body will produce an increase in urea.

An increase of the urea, to such an extent that upon the addition of nitric acid a pulp of nitrate of urea is formed is found:

1. When the diet is principally animal.

2. In acute febrile diseases, until the acme is reached. Urea in this case comes from increased wear of the nitrogenous elements.

3. In diabetes mellitus and insipidus.

Urea is diminished:

1. When the diet is vegetable, and in fasting.
2. In chronic diseases where tissue change is impaired (cachexias).
3. In parenchymatous affections of the kidney, accompanied by uræmia, especially before death (7 gr.!).

The percentage of urea is diminished in urina potus, spastica and diabetes, but if the quantity in twenty-four hours be taken into consideration, it will be found that the urea is usually increased; it is present in normal quantity at least.

II. Uric Acid.

$$C_5NH_4O_3.$$

Uric acid is always found in the urine of carnivora. The healthy adult usually voids from 0.4—0.8 grammes in twenty-four hours.

It is sparingly soluble in (14,000 parts of cold and 1,800 of warm) water, and entirely insoluble in alcohol and ether. This alone speaks for the fact, that uric acid is not present free in the urine, but nearly all of it in the form of the urates.

In a warm solution of normal alkali phosphate, uric acid is much more soluble than in water, because it withdraws from the phosphate part of its base. In this way, then, is produced an acid alkali phosphate and an alkali urate.

Free uric acid, as well as its salts, always appears

colored in the sediment, the intensity depending on the color of the urine.

In order to obtain uric acid from urine, 20 parts of the latter are mixed with one part of hydrochloric acid, and the whole allowed to stand for twenty-four hours. A crystalline powder or membrane is separated, consisting of uric acid, on the bottom and walls of the vessel, and also on the surface of the fluid.

The primary crystal of uric acid is the whetstone, or, better, a rhombic vertical prism. In this form, and its variations we find it also in native sediments. If uric acid is separated from urine by means of hydrochloric acid, the forms are somewhat changed. They seem coarser and more highly colored. Usually there are found under the microscope double whetstones, in the form of a cross; groups of narrow and long whetstones arranged parallel to each other, or like needles, which somewhat resemble a comb, having teeth on both sides. It is rare to find single crystals. If the uric acid which has been precipitated by hydrochloric acid, is separated by filtration, redissolved in potassium or sodium hydrate, and reprecipitated by hydrochloric acid, the result will be a much whiter deposit. Repeating the process, frequently, will finally produce snowy white crystals, even from human urine. Uric acid can also be purified by means of dissolving in sulphuric acid and then precipitating by adding a great quantity of water.

Uric acid or the urates should never be present in fresh urine; when they are, our attention must be drawn to the formation of calculi. In the formation

of gravel and calculi, concrements of uric acid, which are too large for microscopic examination, are passed, and which do not, therefore, permit of an accurate diagnosis regarding their structure. In these cases the chemical test, murexid, will give us positive results.

To make this test, the concrement is pulverized in a small mortar, put into a porcelain evaporating dish, and a few drops of nitric acid and a small quantity of water added. These are heated until the uric acid is dissolved, and the fluids driven off. During evaporation, if uric acid is present, we notice intense red deposits on the walls of the vessel, which disappear when the temperature is sufficiently raised by approximating the lamp to the vessel. When the solution has been evaporated nearly to dryness, upon the addition of a drop of aqua ammonia, the whole contents of the dish appear of a beautiful purple (murexid-purpurate of ammonium); when a drop of a solution of potassium hydrate is added to this, the solution appears violet. This reaction depends upon a change in the uric acid to alloxan and alloxantin, which are converted into murexid by the ammonium.

Instead of using the test, the concrement may be dissolved in potassium hydrate, precipitated by hydrochloric acid and examined under the microscope, the crystals being characteristic for uric acid.

If only a small quantity of fluid is at our disposal, and we wish to test for uric acid, it should be put into a watch glass together with a linen thread; add 6—8 drops of glacial acid, and allow the whole to stand for

twenty-four hours at 15° C., then examine with the microscope to see if crystals of uric acid are deposited upon the thread.

If to an alkaline solution of uric acid, a weak solution of copper sulphate be added, a white precipitate of cuprous urate will be formed. If an excess of cupric oxide be added and the whole boiled, the red cuprous oxide will be precipitated; for oxygen of the cupric oxide is used for the oxidation of the uric acid. We therefore find in the solution, urea, allantoin and oxalic acid. This alkaline solution of uric acid will also reduce nitrate of silver. If the two are mixed in small quantities, a spot will be found upon the filter, black if there is present 1–1000 uric acid, or brownish-yellow if there is 1–500,000.

By means of ozone, in the presence of an alkali, uric acid is converted into urea, ammonia, oxalic acid and carbonic acid; when the alkali is absent, into urea, carbonic acid and allantoin.

When acted upon by various oxidizing agents, uric acid gives rise to a great number of interesting products, most of which can be considered urea in which atoms of hydrogen have been displaced by acid-radicals. It seems that uric acid itself contains the remnants of two molecules of urea.

Uric acid is a bibasic acid, and as a result, two series of salts are formed, neutral and acid.

The neutral salts are more readily soluble in water than the acid salts. Acid sodium-urate requires 124 parts of boiling, and 1150 parts of cold water to dissolve it. Therefore, if we find urates in the sediment,

we know that they are acid salts. On the other hand, if we find urates in solution, especially after the urine has acquired the temperature of the room, we can assume that they are, principally, neutral. This view is supported by the fact that if an urine corresponding to the preceding is decomposed by a strong acid (muriatic or nitric), the whole urine at first becomes cloudy. If this cloudiness is examined under the microscope, we see that it is produced by amorphous points, which are acid urate of sodium. After having stood for some time, the milky cloudiness disappears, and in its stead appears a distinct crystalline deposit of free uric acid. This phenomenon can only be explained by assuming that in the clear urine neutral urates were held in solution, from which, by the addition of acids, some of the base was taken, producing the less soluble acid urates. The acid continuing to act, all the base is taken from the urate, leaving free uric acid.

In the reaction for albumin, when the nitric acid is poured under the urine, it is an established fact that frequently a layer is produced which, by the inexperienced, might be taken for the albumin precipitate. This, however, consists simply of amorphous acid urates, which are changed to uric acid on standing.

The acid urates of sodium and ammonium will find consideration under the heading of sediments. The causes for the increase or diminution of uric acid have not, as yet, found a satisfactory explanation.

Uric acid is considered as a preliminary step toward the formation of urea, although it is not at all prob-

able that all the urea of the body is developed in this manner. From this the increase of uric acid was explained in all those conditions in which oxidation of the nitrogenous excretions is insufficient, either from the presence of too little oxygen or from the increased formation of uric acid, which is too great for the normal quantity of oxygen to dispose of. Many facts, however, do not harmonize with this explanation.

Uric acid, as derivative of protein compounds, has the same importance for the economy as urea. Usually, therefore, we find an increase of uric acid, where urea is excreted in greater quantity.

We find an increase of uric acid:

1. Where a great quantity of food is taken, either animal or vegetable diet, with little exercise in the open air.
2. In acute febrile diseases, where many nitrogenous compounds are decomposed.
3. In diseases of the lungs and heart, accompanied by insufficiency of respiration.
4. In all those cases in which the diaphragm is prevented from performing its function; in large tumors of the abdomen, ascites, etc.
5. In leucæmia, either on account of increased production of uric acid by the diseased spleen, or on account of diminished oxidation by the blood, poor in red corpuscles.
6. In the so-called uric acid diathesis.

A diminution is usually found in chronic diseases of the kidney, diabetes mellitus (occasionally), urina spastica, hydruria and arthritis.

To determine, approximately, the quantity of uric acid in urine, the following may be used: Normal urine of 1020–1024 sp. gr. neither precipitates uric acid nor urates at the ordinary temperature, nor can we detect a precipitate upon using the nitric acid test. If concentration increases, there will be observed in the sediment a small quantity of free uric acid, and the nitric acid test will reveal a narrow layer. In such cases, however, the specific gravity is always increased; therefore, urea, and with it, uric acid, are present in greater quantity. If the quantity is normal, and we find much brick-dust sediment, and also urates in solution, or a considerable sediment of uric acid, the uric acid is increased.

But if the quantity is diminished, this conclusion can not be drawn. In this case, although the urates are present in normal quantity, there may not be sufficient fluid present to hold them dissolved at the ordinary temperature.

For ordinary purposes it is safe to consider uric acid as diminished where urea is. All that has been stated refers to the quantity in percentage. If we wish to have an idea concerning the whole quantity, we must naturally, take the quantity of urine passed in twenty-four hours into consideration. It is best to compare with normal urine. The average quantity is 1500 c. c. We must, therefore, add enough water to make up these 1500 c. c. in twenty-four hours. If we take the quantity in twenty-four hours as 1000 c. c., we must add 500 c. c., or, to 10 c. c. of urine 5 c. c. of water. Two test tubes of equal diameter are selected; into

one is put 15 c. c. of normal urine; into the other, 10 c. c. of the concentrated urine, and to both are added 10 drops of muriatic acid, and then allowed to stand for twenty-four hours. From the precipitate we can easily determine whether the uric acid is increased or diminished in the urine that is compared with the standard. If the quantity is greater than 1500 c. c., the corresponding dilution of the normal urine must be had recourse to.

III. Coloring Matter.

In normal urine there occurs urine indican and a pigment, urobilin. Besides these well known bodies, there are found several other pigments, which, however, have not been thoroughly studied.

(a) Urobilin.

Urobilin is a brown, resinous mass, readily soluble in water, but more readily in alcohol, ether and chloroform. Concentrated solutions are brown, varying from a yellow to a pink. They have no reaction with litmus, by reflected light show a beautiful green fluorescence, and with the spectroscope possess a dark band of absorption between the Frauenhöfer lines *b* and *F*. The fluorescence and spectroscopic appearance become more distinct upon the addition of ammonia and a trace of chloride of calcium. Upon the addition of hydrochloric acid, however, the fluorescence disappears, and the absorption band approaches *F*, becomes fainter and has less marked outlines. If am-

monia is added to the acid solution, its brown or red color is changed to a light yellow, approaching a green. Alkaline solutions show the same absorption band, and, at the same place as neutral solutions.

In order to obtain urobilin, it is advisable to take dark fever urine. It is made strongly alkaline by ammonia, filtered, and then chloride of zinc is added until no precipitate is produced. The precipitate is washed upon the filter, first with cold, then with warm water, until nitrate of silver no longer produces turbidity in the water used for washing. Then it is boiled with alcohol, dried at a moderate heat, the powder dissolved in ammonia and precipitated with lead acetate. The precipitate is then washed a little with water, decomposed with a moderate quantity of alcohol, containing sulphuric acid, and filtered. To the filtrate an equal quantity of chloroform is added, shaken, in order to remove the sulphuric acid, adding fresh water until this shows traces of color. Upon evaporating the chloroform, the urobilin remains in the form of a resinous mass.

According to the researches of Maly, urobilin is a result of the reduction of bilirubin. As Hoppe-Seyler has succeeded in producing a compound identical with urobilin, by means of acting on blood-coloring matter with hydrochloric acid and tin, and as, on the one hand, the injection of substances that destroy the blood corpuscles increases the formation of biliary coloring matter, we can hardly doubt that urobilin is the direct or indirect result of the reduction of haemoglobin, and therefore its increase is of interest to the physician. It is found in acute febrile diseases, and points to an increased waste of red blood corpuscles.

Urine which, without any further preparation, shows a greenish fluorescence upon the addition of ammonia and chloride of zinc, and the characteristic absorption line, can be put down as rich in urobilin.

Scherer's urohaematin, Heller's urophaein, Thudicum's urochrome, etc., are bodies for whose purity we have no guarantee; indeed, for urochrome and urohaematin, Maly has shown that both contain much urobilin.

(B) Urine-Indican.

Since the time of Heller, it is known that an addition of hydrochloric acid to urine will produce a peach-blossom red, violet, or deep blue discoloration. The red he attributed to urrhodin, the blue to uroglaucin, and the coloring matter from which both arise, and which he conceived to be yellow, he called uroxanthin. Uroglaucin was also found in spontaneously putrid urine, and has been identified with the indigo of plants. Uroxanthin was therefore considered the same as indican, the mother substance of indigo white found in plants. Recent investigations have shown that the body which forms the indigo found in urine is not identical with plant-indican. We will therefore call it urine-indican.

This substance can be obtained pure by means of precipitating with lead acetate, decomposing with ammonia; this precipitate, suspended in alcohol, is subjected to a current of sulphuretted hydrogen gas, then filtered from the lead sulphide, evaporated by gentle heat, finally in vacuo over sulphuric acid. More complicated methods are known. For particulars, see Hoppe-Seyler, Chemische Analyse, p. 191.

Urine-indican is not a glucoside, because, upon splitting it up no sugar is found; it is a bi-sulpho acid on account of the treatment with hydrochloric acid's giving large quantities of free sulphuric acid. In the uncombined condition, these acid-ethers are unstable, and putridity, as well as the action of mineral acids, decompose them. Simultaneous, in both instances, there is an oxidation, so that the formation of indigo does not depend solely upon a splitting up. The one product is indigo; a second is a red body, whose sublimate condenses to fine red needles, which may be identical with Heller's urrhodin. Upon the quantity of these two products depends the color which is produced upon the addition of hydrochloric acid to urine.

When concentrated sulphuric acid is allowed to drop into urine from some height, the mixture is usually colored more or less dark red. This seems to depend upon various products (probably the splitting up of urine coloring matter). In the presence of sugar, albumin and constituents of the bile, undoubtedly all participate in the splitting up, so that the mixture may become opaque and brownish black (Heller's urophæin test). As this mixture generates a considerable amount of heat, many substances, such as iodine, the odoriferous oil of cubebs, of sassafras, etc., escape, and are detected by the smell. In parenchymatous purulent processes in the bladder, an exceedingly offensive and penetrating odor is generated.

The oldest test for indican is the uroxanthin test of Heller.

1. This is carried out in the following manner: There is poured into a beaker 3–4 c. c. of pure hydro-

chloric acid, and into this are dropped from 10–20 drops of urine, and the mixture is stirred with a glass rod. Under normal conditions, there is only sufficient indican present to give the mixture a light yellowish-red tint. If, however, the acid becomes violet or blue, then the quantity of indican is greater than normal. The more indican there is present, the more rapidly does this change take place, and sometimes 1 or 2 drops of urine are sufficient to give a blue tint to 4 c. c. of hydrochloric acid. If, after 1 or 2 minutes, no violet is perceived, indican is not increased, even should the mixture turn dark reddish-brown after standing from 10–20 minutes.

In the urine of jaundice, the biliary coloring matter must first be precipitated with acetate of lead, and the whole be filtered before performing the test.

The color in the uroxanthin test is, unfortunately, of little value, as it not only represents the quantity, but also the varied capability of decomposition of indican; how inconstant this is, is proven by the fact that urine-indican produces at one time more indigo blue, and at another, more indigo red. Above all, it must be observed that albumin with hydrochloric acid, especially when heated, or the action has gone on for some time, shows a violet color. Notwithstanding this, the dark blue color may be looked upon as a sign of increase in indican.

2. 10 c. c. of urine are mixed with equal quantities of hydrochloric acid, and then either a saturated solution of calcium chloride, or simply chlorine water is dropped into the mixture, and the color is observed (Jaffe's test).

3. Heat about 5 c. c. of urine moderately, with double its quantity of nitric acid, then shake with chloroform, which will take up the indican, and examine this chloroform extract with the spectroscope (Stokvis' test).

If indol is introduced into the system, indican is very much increased; the same occurs if the small intestine is ligated. The pancreas digestion produces, in its last stage, indol; by tying the intestine this is increased, absorbed and finally produces an increase in the urine-indican. The albumin of food, then, is a source of indican. In the ordinary putrefaction of albumin, indol is generated. On the other hand, it is becoming more probable that a part of the albumin in the body, as the result of a fermentative process, is divided up as it would be by putrefaction outside of the body. The albumin of the tissues, then, is the other source of indol, and therefore of indican. In this way may be explained how, in fasting, indican does not entirely disappear from the urine, being formed at the cost of the disintegrating tissues.

Indican is increased; in meat diet, in Addison's disease, in cholera, in cancer of the liver; it is enormously increased in all diseases that produce a closure of the small intestine (incarceration, invagination, etc.); not so much in obstruction of the large intestine; ordinary constipation. It is very much increased in cancer of the stomach and peritonitis. In disease of the kidney, with the exception of the granular kidney, indican is not much increased. In general, chronic consumptive and inanition-processes increase

it rather than acute diseases. Fever does not cause the same increase in indican that it does in urobilin.

Increase of urine-indican in lesions of the central and peripheral nervous system has only been determined by means of the reaction for uroxanthin, and therefore awaits further, more accurate investigation to make this result positive.

IV. Other Normal Organic Constituents.

We will only give brief mention of the remaining organic constituents, as they possess, thus far, very little value for purposes of diagnosis.

Kreatinin—the strongest base in the body—is passed in the same quantity as uric acid. The average quantity for twenty-four hours is between 0.6–1.3 grammes. In vegetable diet the quantity is smaller than in animal diet. It has been found increased in pneumonia, intermittens and typhus; diminished in inanition and advanced disease of the kidney.

Hippuric Acid is found principally in the urine of herbivora. In human urine it is found in very small quantities. The average quantity is between 0.5 and 1.0 grammes in twenty-four hours. After eating certain kinds of fruit (green gages, whortleberries, etc.), and after the administration of benzoic acid, hippuric acid is increased. This is also the case in febrile diseases and in diabetes; it is diminished when exclusive meat diet is used. If the quantity is increased very much, hydrochloric acid will cause a precipitate of hippuric acid, just as it would of uric acid.

Xanthin and the phenol-producing, disulphonic acid, are found in very small quantity in the urine. The former can only be obtained from several hundred liters of urine, in sufficient quantity for qualitative tests. The presence of phenol-forming substances is indicated by the phenyl reaction of the urine when it has previously been acidulated with a strong

mineral acid. If, however, tartaric acid is used, the distillate of normal urine shows no phenol reaction, proving that phenol (carbolic acid) only exists in urine in a combined state.

Mesoxalic Acid is found in very small quantity. It is the result of the indirect oxidation of uric acid, which produces parabanic acid; this, taking up water, is converted into mesoxalic acid, and, finally, when boiled with water, into urea and oxalic acid.

Oxalic Acid is found in the sediment in the form of its calcium salt.

Concerning the presence of *Sugar* in normal urine, authorities are divided. At all events, a substance is found in normal urine which, in common with the urates, will reduce copper sulphate in alkaline solutions.

In normal urine the existence of *Lactic Acid* has not been positively decided upon. In pathological urine, two kinds of lactic acid, occurring in fermenting urine of diabetes, and sarcolactic acid, after phosphorous poisoning, in acute yellow atrophy of the liver, in malacosteon and trichinosis.

B.—Normal Inorganic Constituents.

1.—Chlorides.

In human urine we find the chlorides limited to the chloride of sodium, to the almost entire exclusion of chloride of potassium. The average quantity found in the urine of a healthy man for twenty-four hours, is from 10 to 16 grammes (6–10 gr. chlorine). After urea, chloride of sodium is the principal constituent of urine—indeed, in accordance with this fact, urine possesses a salty taste. If a drop of urine be evaporated on a slide, and put under the microscope, be-

sides the rhombic plates of urea, chloride of sodium will be found in flat octohedra or incompletely developed crystals of the tessular system.

It is frequently important for the physician to find out easily and quickly whether or not the chlorides are increased. This can be done in the following manner:

If a solution of common salt is decomposed by nitrate of silver, a white precipitate of chloride of silver is produced:

$$NaCl + AgNO_3 = NaNO_3 + AgCl.$$

But if we have a solution which also contains phosphates, as urine, we must acidulate with a little nitric acid before making the test, so as to prevent the phosphoric acid from precipitating with the silver, thus increasing the latter. An unimportant inaccuracy is produced by simultaneous precipitation of uric acid; this, however, can not be prevented. The nitric acid prevents the formation of phosphate of silver, but not of the insoluble chloride. If a solution of nitrate of silver of constant strength (1 in 8) is taken for this test, and single drops are added to $\frac{1}{2}$–1% solution of common salt (as urine), they will fall to the bottom of the vessel in the form of cheesy masses, not to be subdivided by shaking, and never producing cloudiness. If we have a very dilute solution, $\frac{1}{10}$% and under, no masses are formed, but the entire fluid presents a uniformly milky and turbid appearance.

This method can be utilized for the examination of urine in the following way: Fill a wine glass half

full of urine which has been acidulated with nitric acid, and add one or two drops of the silver solution. If the drops come down as cheesy globules, the chlorides are not diminished; if a milkiness is produced they are very much diminished; if this is wanting, they are entirely absent.

The test for albumin can be made to serve as a test for salt. Stir nitric acid with the urine, and then add the nitrate of silver. If much albumin is present, the coagulum must be removed by filtration before performing the test for the chlorides.

The chlorides are diminished:

1. In all acute febrile diseases, especially if combined with serous exudations or watery passages. The quantity of chlorides is in direct ratio to the quantity of urine, and in inverted ratio to the specific gravity and quantity of urea, until the acme of the febrile process is reached.

As a rule, the kidney excretes only the excess of chlorides. In inflammatory processes, common salt frequently collects in the exudations (pleuritis). On the whole, in connection with acute processes, it may be said of the chlorides, that their increased diminution indicates an increase of the disease, and *vice versa.*

In pneumonia, for instance, the chlorides may be entirely absent without our being able to account for it by their diminished introduction into the system.

In typhus or meningitis they are diminished, but not absent. Absence of chlorides always indicates a grave affection.

3. In chronic diseases, with diminished digestive powers, or dropsy.

Increase of the chlorides is observed:

1. When much salt is introduced.

2. When much physical or mental labor is performed.

3. During paroxysms of fever and either before or after. Throughout the twenty-four hours this is compensated for, so that the whole quantity is normal, or even sub-normal.

4. In diabetes insipidus.

5. In dropsy, as soon as diuresis has been established, so that the pent-up chlorides suddenly find escape.

2.—Phosphates.

The whole amount of phosphoric acid passed in twenty-four hours is between 2.3 and 3.8 grammes; in healthy men the average is 3.5 grammes. The diurnal variations can be very great. The quantity increases after the meal until evening (maximum), and falls during the night until next morning (minimum).

We find an increase of phosphoric acid in urine:

1. After the introduction of phosphorus, phosphoric acid, or the soluble phosphates into the organism.

2. When the diet is principally animal, and especially when food is taken that contains more or less prepared phosphoric acid as brain.

3. In all acute febrile diseases (not always).

A diminution is found in all urine of low specific

gravity: urina potus, urina spastica, etc., in kidney and in heart disease, with diminished urine; in serious disturbances of digestion, and in chronic brain troubles (except epilepsy).

Phosphoric acid PO_4H_3 is a tribasic acid, *i. e.*, the three atoms of hydrogen can be displaced by metals.

In urine this acid is partially bound by the earthy, partially by the alkaline bases (earthy and alkaline phosphates).

(*d*) The earthy phosphates, *i. e.*, of calcium and magnesium are found, normally, in very small quantity (0.9–1.3 grammes in twenty-four hours). Magnesium phosphate is present in about double the quantity of calcium phosphate. In acid urine we find these salts in solution; in alkaline urine, however, they are found in the sediment.

Phosphoric acid forms, with calcium, three salts:

The neutral:
$$\begin{array}{l}\mathrm{PO}\left\{\begin{array}{l}\left.\begin{array}{l}\mathrm{O}\\ \mathrm{O}\end{array}\right\}\mathrm{Ca}\\ \mathrm{O}\end{array}\right.\\ \qquad\qquad\}\ \mathrm{Ca}=(PO_4)_2Ca_3\\ \mathrm{PO}\left\{\begin{array}{l}\mathrm{O}\\ \left.\begin{array}{l}\mathrm{O}\\ \mathrm{O}\end{array}\right\}\mathrm{Ca}\end{array}\right.\end{array}$$

The single acid:
$$\mathrm{PO}\left\{\begin{array}{l}\mathrm{OH}\\ \left.\begin{array}{l}\mathrm{O}\\ \mathrm{O}\end{array}\right\}\mathrm{Ca}+2H_2O=PO_4HCa+2H_2O\end{array}\right.$$

The double acid:
$$\begin{array}{l}\mathrm{PO}\left\{\begin{array}{l}\mathrm{OH}\\ \mathrm{OH}\\ \mathrm{O}\end{array}\right.\\ \qquad\qquad\}\ \mathrm{Ca}+H_2O=(PO_4H_2)_2Ca+H_2O\\ \mathrm{PO}\left\{\begin{array}{l}\mathrm{O}\\ \mathrm{OH}\\ \mathrm{OH}\end{array}\right.\end{array}$$

The last combination is found dissolved in urine. A double magnesium-phosphate is not known. The

single acid salt is said to be held in solution in urine by free acid (?).

The reaction for the soluble earthy phosphates is performed by alkalies (sodium, potassium, or ammonium).

In calcium phosphate, acid is withdrawn thus:

$$3[(PO_4H_2)_2Ca]+12KOH=(PO_4)_2Ca_3+4PO_4K_3+12H_2O.$$

With magnesium-phosphate, on the other hand, ammonium-magnesium phosphate is formed if ammonium is used:

$$PO_4HMg+NH_3+6H_2O=PO_4Mg(NH_4)+6H_2O.$$

The crystalline form will be described in connection with the sediments.

In order to test for the earthy phosphates, fill a test-tube one-third full with clear urine, add a few drops of caustic potassium or ammonia, and heat until the earthy phosphates precipitate in flakes; put the test-tube on a stand for 10–15 minutes, until the precipitate is deposited, and then judge of the quantity. If we have used a test-tube about 16 c. long and 2 c. in diameter, a layer of 1 c. in depth will represent the normal quantity; if the layer is 2–3 c. deep, the earthy phosphates are increased; if only a few flakes are present. they are diminished.

In normal urine they form a white precipitate; if the urine contains abnormal coloring matter, the color of the precipitate will be determined by it. Blood coloring matter makes the precipitate blood-red or dichroic; vegetable coloring matter, of rhubarb or

senna, etc., pink or blood-red; biliary coloring matter, yellowish-brown and uroërythin gray.

Diseases of bone, malacosteon, rachitis, etc., extensive periostitis, chronic arthro-rheumatic processes; the introduction of mineral waters rich in calcium, medicines and exclusive meat diet (not constant), produce an increase of earthy phosphates.

A diminution is observed in diseases of the kidneys.

In alkaline urine the earthy phosphates are found in the sediment.

(*b*) Alkali phosphates are represented (principally) by the acid phosphate of sodium and of potassium (traces).

The tribasic phosphoric acid forms three alkali salts, depending on 1, 2 or 3 atoms of hydrogen being displaced by the metal:

PO_4H_2Na	PO_4HNa_2	PO_4Na_3
(Di-hydrogen Sodium Phosphate).	(Hydrogen Di-sodium Phosphate).	(Tri-sodium Phosphate).

Only the first has an acid reaction, and its presence produces the acid reaction of urine. The other two have an alkaline reaction. All are readily soluble in water (in contradistinction with the earthy phosphates), even in alkaline water.

Of the entire phosphoric acid found in urine, two-thirds are bound to the alkalies.

The reaction is best performed with the magnesia fluid (see Chap. IV., No. 10). If we want to examine for all of the phosphoric acid in urine, we add to 10 c. c. urine 3 c. c. of the magnesia fluid. There is produced a precipitate which is made up principally of

ammonium-magnesium phosphate, with which amorphous calcium-phosphate is mixed. If the entire fluid becomes milky, the alkaline phosphates are present in normal quantity. If the precipitate becomes so dense as to give to the fluid the consistency of cream, then the phosphates are increased. If the fluid is simply turbid and very transparent, then there is a diminution.

This is a reaction for the entire phosphoric acid, but as the earthy phosphates are present only in such small quantities, they need either not be taken into consideration, or, with a little practice, one learns to subtract the quantity found by means of the test for the earthy phosphates from the result obtained by this test.

If the earthy phosphates are present in very great quantity, they must be precipitated by ammonia, the urine filtered, and to this the magnesia fluid must be added.

4.—Sulphates.

The sulphates found in urine are the neutral sulphates of sodium and potassium.

The sodium salt, as is the rule every-where, is found in greater quantity than the potassium salt. The quantity of sulphuric acid passed by the healthy adult in twenty-four hours, is between 1.5 and 2.5 grammes—average 2.0 grammes.

The reaction for sulphuric acid is performed in a manner similar to that for phosphoric acid. Into a test-tube is put 10 c. c. of urine, a few drops of hydrochloric acid are added in order to prevent barium-

phosphate from being precipitated, then add one-third the quantity (3–4 c. c.) of a solution of chloride of barium. The reaction takes place according to the following formula:

$$BaCl_2+Na_2SO_4=2NaCl+BaSO_4,$$

Sulphate of barium being the desired precipitate. The solution of chloride of barium can be previously acidulated with hydrochloric acid (Chap. IV., No. 7), this precluding the necessity of acidulating the urine.

If there is produced an opaque, milky turbidity, then the sulphates are present in normal quantity; if the consistency is changed to that of cream, then they are increased, and if only a translucent turbidity is produced, the sulphates are diminished.

A very pretty quantitative test has been described by J. Vogel, which depends upon the above reaction, and is performed by taking 100 c. c. of the urine (2.00 grammes of sulphuric acid being voided in twenty-four hours with a quantity of 2,000 c. c.) and adding sufficient chloride of barium solution to satisfy one-half the sulphuric acid contained in the 100 c. c. of urine—*i. e.*, 0.05 grammes. If, upon the further addition of the test solution, no precipitate is formed, the sulphates are diminished. If a precipitate is produced, add the same quantity of the test solution that was originally employed, and again test. If no precipitate is produced, the sulphates are normal, but if a precipitate is produced upon the further addition of the fluid, the sulphates are increased.

An increase of sulphuric acid or the sulphates is observed:

1. After the introduction of sulphuric acid, its

soluble salts, of sulphur combinations, or of sulphur itself, into the organism.

2. In exclusive meat diet, the sulphur of the albumin being oxidized to H_2SO_4.

3. In acute febrile diseases, accompanied by free excretion of urea. Increase in the sulphuric acid must, in this case, be referred to an increased waste of those constituents of the body which contain sulphur. The highest degree is noticed in meningitis, encephalitis, rheumatism, and affections of the muscular system.

A decrease in the sulphates occurs in exclusive vegetable diet, in the beginning of typhus and (in percentage) in all those urines that show diminished specific gravity.

Other inorganic substances that have been found in urine are; ammonia, iron and silicic acid. Traces of all, only, are found, but for the first, Duchek claims that as fevers increase, so ammonia increases, to diminish in reconvalescence.

C.—Abnormal Constituents.

1.—Albumin.

Normal urine should never contain albumin. In pathological conditions, notably in diseases of the kidney, it is frequently found in great quantities.

After the taking of much egg albumin, Cl. Bernard, Becquerel and others have observed albumin in otherwise perfectly healthy urine. Serum albumin (up to 0.1%) may be present in the urine of perfectly healthy persons. We have reported several cases (Wiener Med.

Presse, 1870,), as well as Vogel. The cause for this is unknown. The urine, in these cases, was somewhat concentrated, very acid, and contained more urea and uric acid than normal. In the sediment we sometimes found nothing, sometimes crystals of uric acid or oxalate of lime. It is probable that this albuminuria, periodic and presenting variable quantities of albumin, was due to the chemical composition of the urine. It might also be attributed to certain abnormal nervous conditions of the kidney. At all events, these cases are of such rare occurrence that the presence of albumin must be considered abnormal.

Why albumin is not found in the healthy condition, is best explained by the mechanical theory of Ludwig.

Graham divides all bodies into crystalloids and colloids, the former diffusing readily through animal membranes; the latter diffusing with difficulty, or not at all, and being non-crystallizable. This division, applied to albumin, will show that serum albumin is a colloid, for it does not crystallize, nor does it pass through animal membranes, unless increased pressure is applied. The crystalloids passing so readily through membranes, and the colloids with such difficulty, it is natural to assume that the molecule of albumin must be larger than that of any crystallizable salt. The probability for this increases when we consider the facility with which foam is produced in albumin solutions, and also its complicated chemical structure. The latter finds expression in the formula $C_{216}H_{169}N_{27}S_{3}O_{68}$.

According to Ludwig, we have in the glomerulus, a

process of transudation, while throughout the course of the tubules we have one of diffusion. The two fluids, blood and the water of urine, are always found separated by animal membrane. These septa have the property of allowing the crystalloid substances of the blood (salts, urea, etc.) to pass through readily, but not the albuminoids, under the conditions of pressure in the kidneys, therefore we can not expect to find albumin in normal urine.

If we find albumin, then the blood pressure in the vessels of the kidney is usually increased (passive hyperaemia, valvular heart disease, amyloid degeneration of the vessels, etc.) or the membrane, in some place, has become pervious (parenchymatous nephritis, Bright's disease).

Albumin is found in urine most frequently as serum albumin and paraglobulin. If other fluids that contain albumin (blood, pus, exudations, etc.) are present in the urine we will find that form of albumin which is characteristic of these. Fibrin is found in copious hemorrhages and croupous affections of the urinary apparatus.

True fibrinuria, a so-called coagulable urine, that is said to occur frequently in Isle de France, is, with us, a very rare occurrence. We observed this, temporarily only, in three cases of papillomatous tumors of the bladder. But we not infrequently find urine having the consistency of honey or syrup, depending, however, upon pus dissolved in alkalies, not upon fibrin. This form of urine becomes thin upon the addition of water, and acetic acid produces a white precipitate of

albuminate, produced by the action of ammonium carbonate on the serum-albumin of pus.

For albumin there are many characteristic reactions; for urine, however, two are of especial value — the concentrated nitric acid test, and boiling.

1. To carry out the nitric acid test, put about 10 c. c. of urine into a glass (best a wine or sherry glass) and pour under it pure, colorless, concentrated (not fuming) nitric acid. The reagent is poured under the urine by means of holding the glass containing the nitric acid at an angle with the one containing the urine, and allowing the acid to flow gently along the side of the latter. At the place where the acid and the urine touch, when albumin is present, a band-like zone appears, having both upper and lower boundary lines sharply defined. This can only be mistaken for resins (copaivic acid) or the urates; the latter, when present in great quantity, also precipitate upon the addition of nitric acid. This layer, however, does not appear where the urine and acid touch, but higher up; neither is its upper margin sharply defined, but looks more like a cloud of smoke, slightly curly in the middle. If albumin and the urates are present at the same time, two white layers, superimposed, will be obtained. The lower one will be albumin, the upper one, urates. They are separated from each other by a layer of clear urine.

The precipitate produced by resins is dissolved by the addition of a few drops of alcohol.

If this test is performed with normal urine, there will be observed between the urine and the nitric acid

a brown ring of coloring matter which, in a few minutes, increases in intensity. We now comprehend how, in fever urine, rich in coloring matter, which at the same time may contain albumin, the ring of albumin will be, not snowy white, but more or less brownish. If much indican is present the albumin frequently appears pink or violet; in the presence of blood-coloring matter, red and with biliary coloring matter, not decomposed, of a green color. If urine is very much concentrated, there will be produced a copious crystalline deposit which, under the microscope, will reveal itself as nitrate of urea. Urine, rich in uric acid, might produce free uric acid in the form of yellowish whetstones, which can be readily differentiated from the preceding precipitate by its insolubility in water.

If urine contains much carbonic acid, either on account of its being alkaline and having much carbonate of ammonia, or being neutral or acid, having sodium carbonate or free carbonic acid gas (as is frequently the case during the use of mineral waters), then there will be observed, upon the addition of nitric acid, an effervescence of the fluid.

If this test does not convince to satisfaction, then the next must decide; indeed, it is always best to perform both tests.

2. The test by boiling is performed in that we take 8–10 c. c. of urine, if it be acid, and boil it in a test-tube. It is always safer to add 1–2 drops of acetic acid. A flaky cloudiness indicates albumin. If the urine is neutral, faintly acid or alkaline, a precipitate

may show itself on boiling, which, upon the addition of acetic acid, again dissolves. This is not albumin, but the earthy phosphates that have been held in solution by carbonic acid gas, which, being driven out by heat, can no longer dissolve them. One thing which has only been done as a precaution in acid urine, must always be done in alkaline or neutral urine to prevent deception, viz: acidulate the urine.

In this test, albumin is not only simulated, but in alkaline urine, may entirely escape detection. The nitric acid test frequently fails us here, on account of the effervescence produced by the reaction upon the carbonates. If we do not acidulate, the alkali present may be sufficient to change the albumin to alkali-albuminate, which does not precipitate upon boiling. If we are not careful with the addition of acetic acid we may err on the other side, producing acid-albumin, which can not be precipitated by boiling.

In the presence of very small quantities of albumin, its detection becomes a difficult matter if the urine is already cloudy, or does not come through the filter clear.

Alkaline urine is already more or less turbid, contains no earthy phosphates in solution, and must always be clarified before proceeding to test for albumin. In order to do this, the urine must be boiled with one-fourth its volume of potassium hydroxide (Chap. IV., No. 5,) and filtered. If the filtered urine is not clear, 1–2 drops of the magnesia fluid must be added, and the urine again heated and filtered. If this is then carefully acidulated with acetic acid, the

slightest turbidity of albumin will be detected. This becomes more distinct when ferro-cyanide of potassium is added to the already acidulated urine; white flakes of albumin will then be noticed on the bottom of the vessel.

It is advantageous to know other tests.

(*a*) Acidulate the urine with acetic acid, add an equal volume of a cold saturated solution of sodium sulphate, and boil.

(*b*) Into filtered urine there is dropped saturated solution of picric acid. If cloudiness is produced, albumin is present (Galippé's test). Only the cloudiness that is produced instantly is decisive.

Albumin is found in urine:

1. When the blood-pressure in the Malpighian tuft is greater than normal. This occurs in all anomalies of circulation (valvular lesions of the heart, passive hyperaemia, amyloid and atheromatous processes in the arteries, etc.).

2. In all those diseases in which a change in the diffusion-membrane, *i. e.*, the walls of the tubule with its epithelium and its arterioles and capillaries, can be demonstrated (parenchymatous nephritis, Bright's disease, etc.).

3. When there is mixed with the urine, blood, pus or any other fluid containing albumin (false albuminuria).

4. Occasionally in hydraemia (disturbance of nutrition in the capillaries).

NOTE.—High fever seems to produce true albuminuria. It is not uncommon to find albumin in the urine of patients

suffering with pneumonia, typhoid fever, remittent fever, or severe attacks ulcerative sore throat. The diagnosis of diphtheria, not being an easy one, the latter instance might be referable to an attack of diphtheritis, having been called angina ulcerosa. But the two former conditions leave no doubt but that albuminuria does occur in some febrile conditions. If a post mortem be made upon a patient dying from either of the two conditions named above it will be surprising to find how little change can be observed in the kidneys. The only thing to be found will be cloudy swelling of the epithelium, which is frequently observed without having produced albuminuria intra vitam. Two explanations can be given for the appearance of albumin in the urine: the first, by Gerhardt, that the secretion of urine with the temperature of the blood at 104° F. at least, must be abnormal; the second, that the specific cause of the fever has acted upon the epithelium of the kidney, and thus made the transudation of albumin a possibility. It is said that albuminuria is produced transitorily after epileptic attacks, the quantity of albumin varying with the intensity of the attacks, in that it is greater after complete, or less after incomplete seizures.

It is also thought (Vogel) that albuminuria can arise from the formation in the blood of a peculiar kind of albumin, endowed with different properties of diffusion, being even able to pass through the perfectly intact membrane. We have never been in the position, however, to verify this view.

In true albuminuria it is important to be able to determine the quantity of albumin excreted in twenty-four hours, for only by means of this can we determine whether or not improvement is taking place. The most accurate quantitative analysis of albumin is made by means of the scales or the polari-

scope (Chap. V.). These methods, however, are too laborious, and consume too much time for the practicing physician, and we therefore desire a method by which we are enabled to state when albumin is present in great (1–2%) or in small (½%) quantity. This can be accomplished, with a little training, by observing the albumin zone in the nitric acid test. If this zone is faint, whitish, not granular; if it is more or less translucent, and only to be distinguished as a sharply defined band when placed against a dark background, and, above all, is only between 2 and 3 m. m. high, we may know that albumin is only present in very small quantity (below ½%, usually 1 part in 1,000). If this zone is between 4–6 m. m. high, white, opaque, perceptible without a dark background, and granular, then albumin is present in moderate quantity (¼–½%). But when, upon the addition of nitric acid, the albumin precipitates in flakes or granules, and sinks to the bottom in small masses; when, upon stirring this mixture with a glass rod, the urine has the appearance and consistency of cream, then the quantity of albumin is very great (1–2% and more).

Similar results can be obtained with the boiling test.

Fill a test-tube one-third full with clear, filtered urine (if alkaline, acidulate with acetic acid). A very slight turbidity, which causes the urine to appear translucent after boiling, and simply makes it opalescent, indicates a small quantity of albumin. If, on boiling, the urine is milky, if the albumin separates in fine flakes, and upon settling, makes a layer at the

bottom of the test-tube of a finger's height, then albumin is present in moderate quantity. But if the albumin coagulates in coarse flakes, and where the flame touches the tube, instead of from the upper surface of the fluid, as before; and if the urine appears thick, like cream, after boiling, then albumin is present in very great quantity.

To compare the quantity of albumin of one day with that of another, boil in test-tubes of equal diameter, taking equal quantities of urine, and compare the height of the sediments. It is better to use glass tubes of equal diameter, closed with corks wrapped in wax paper. After twenty-four hours we can measure, with a rule, the depth of the albumin layer.

The preceding are short directions for approximate analysis, but they must be frequently exercised, and only he who has made himself perfectly familiar with the appearances can draw reliable conclusions.

What has been said is true for the majority of cases, where the principal quantity of albumin is serum albumin.

At the same time, or independently, we frequently find modifications of albumin, of which the most important is globulin (perhaps myosin).

Peptone is found in every urine containing albumin; in diseases in which there is a very high temperature it is sometimes found, even without the presence of albumin.

In order to detect globulin, we dilute the urine until it has reached a specific gravity of 1002. Then we carefully add very dilute acetic acid (it is soluble

in the concentrated acid). There usually appears a cloudiness. In order to precipitate all the globulin, allow a slow current of carbonic acid gas (bubble after bubble) to pass through the urine for 1–2 hours. If allowed to stand for a time, the globulin separates in the form of a white powder. The fluid can then be tested by the other methods for serum albumin. If the sediment is made up of globulin, it must be soluble in a few drops of concentrated solution of common salt.

Globulin is found in considerable quantities in catarrh of the bladder, acute nephritis, and especially in the amyloid kidney, whilst it is said that in chronic Bright's disease it is present in very small quantity, or even entirely absent.

2.—Sugar.

$$(C_6H_{12}O_6)+H_2O.$$

The sugar of urine (identical with grape sugar) is, according to Brücke, a normal, constant constituent, but it occurs in such small quantity that not even a slight yellow precipitate is noticed when Trommer's test is used, a discoloration only being observed. In abnormal urine, we frequently find so much sugar as to sweeten its taste, especially in diabetes mellitus is this the case. Clothes which have been moistened with such an urine, look, after the water has evaporated, as if they had been dipped in honey.

The sugar of urine crystallizes in watery concre-

ments, consisting of cauliflower leaflets. Of the many tests, the following are usually sufficient:

1. *Heller's Test.*—Mix urine in a test-tube with one-half its volume of potassium or sodium hydrate solution (1 to 3), and boil. First, the earthy phosphates are precipitated; they can be filtered when present in very great quantity. As soon as the fluid is heated, its color changes to lemon, yellowish-brown, or brownish-black, according to the quantity of sugar contained. If a few drops of nitric acid are added to this mixture, the dark color will disappear and an odor of caramel become perceptible. If the urine contains much albumin, it is advisable to remove it first by boiling.

If the urine is highly colored, which rarely occurs in diabetes mellitus, it can be decolorized with sugar of lead solution (the sub-acetate precipitates a small quantity of sugar), or by filtering through animal charcoal. The latter must afterward be washed with water, because it will retain much sugar.

If this change in color takes place while the urine is cold, then biliary coloring matter is usually present. This change will even appear when the coloring matter is already decomposed, *i. e.*, when neither Gmelin's nor Heller's tests will indicate its presence. In this case this test, especially when the addition of sulphuric acid produces a very dark color, is a very good one for biliary coloring matter.

According to Bädecker, if urine is mixed with caustic potassa and exposed to the air, there gradually appears a brown discoloration, the urine absorbing much oxygen and containing a body which he called alkaptone. This, like

sugar of urine, reduces copper, but not bismuth salts. Probably this body is pyro-catechine.

A beautiful reaction is produced by Mulder's test. Mixing urine with a solution of indig-carmine, first made alkaline with sodium carbonate and boiling, the blue mixture first becomes green, then purple, and finally yellow. Shaking the boiling mixture and exposing to oxygen, it again comes back to the original blue.

2. *Trommer's Test.*—As before, mix with the urine caustic potassa or soda solution, and add drop by drop, shaking constantly, a solution of copper sulphate (1 to 10) until a clear, blue fluid is obtained. Then heat over a lamp. If sugar is present, reduction of the oxide of copper takes place in the following manner: First, yellow cuprous hydrate is precipitated; this losing its water, leaves red cuprous oxide. If the test-tube is put aside, and we wait a few minutes, there will be observed a metallic mirror covering the bottom of the tube. Albumin must be removed by coagulation. If this is forgotten, a violet color, upon the addition of the reagents, will be a reminder of its presence. If neither sugar nor albumin is present, then we get a turbid grayish green fluid, but no reduction of the oxide.

Large quantities of creatinin, peptone, etc., can prevent the precipitation of the cuprous oxide.

3. *Bœttger's Test.*—Mix the urine with the alkali, as above, then add as much bismuth—a mixture of basic bismuth nitrate $(BiO)NO_3+BiO, OH$ with bismuth nitrate $(BiO)NO_3+H_2O$—as will cover the end of a knife-blade, and then boil. After a time, a mirror of

bismuth appears on the test-tube. If small quantities of sugar are present, then the bismuth is only colored gray, because only a part of it is reduced—the reaction may even be covered over by the excess of bismuth.

If albumin is present, this must be removed, otherwise bismuth-sulphide may be produced, which may be mistaken for an oxide of bismuth. In order to be certain, it is well to add to a portion of urine that has been made alkaline, acetate of lead; if a black precipitate is formed, it is conclusive evidence of the presence of a sulphur compound.

Brücke recommends, in order to remove all disturbing substances, Frohn's reagent (1.5 grammes precipitated, unwashed bismuth nitrate are heated to the boiling point with 20 grammes of water, then 7.0 grammes of iodide of potassium, and finally 20 drops of hydrochloric acid added). A modification has been proposed by Maschke, he using a solution of tungstate of soda.

Heller's test is the simplest and the best, and has the advantage that with it, one skilled in its use, can tell the approximate quantity of sugar present. Second comes Bœttger's test, for when no albumin is present, no other substance except sugar will reduce the bismuth. Trommer's test is least reliable, for many other substances, when present in the urine in large quantities, will reduce the copper salt: uric acid, the urates and hippuric acid. Many specimens of urine from patients with acute febrile diseases, where the urates are present in great quantity, are diagnosticated as containing sugar, especially if reliance is

placed on the yellow discoloration, not waiting for the precipitate of cuprous oxide. In all cases, the most reliable tests are fermentation and the polariscope, both, however, too laborious for the practitioner.

If the presence of sugar has been demonstrated, it is of equal importance to determine the quantity present, and the amount passed in twenty-four hours. The exact quantitave tests will be discussed hereafter —they alone are reliable. The quantity has been approximately determined by the specific gravity; the higher this is, the more sugar is supposed to be present. This, however, is only true for a pure solution of sugar, not for so complex a fluid as urine, and Bence Jones has shown that the method can not even be utilized for rough estimates.

The second method is that of Vogel; it depends upon the intensity of color produced by the potassa test, and is very useful to the practitioner.

If we make solutions of grape sugar, varying in strength, and test them in test-tubes of equal diameters, a scale can be easily constructed which will suffice for ordinary rough estimates.

Mix two parts of the solution with one part of liquor potassa, and boil. A 1% solution will give a canary-yellow; a 2%, a dark amber; a 3%, a dark rum, and a 10% solution will become dark brown and opaque, while all other solutions are more or less transparent.

Taken in connection with the specific gravity, this test is very useful, as diabetic urine is usually very pale in color.

Sugar occurs in large quantities only in one form of disease: glycosuria. It is found temporarily in certain injuries of the brain, and is said to appear in very small quantities in the urine of acute febrile diseases, spontaneous gangrene, pneumonia, typhus, rheumatism, acute encephalitis, in diseases of the nervous system, especially of the cord, in cachexias, and similar processes; also after the introduction of turpentine, nitro-benzole, nitrite of amyl, etc.

Neukomm and Vogel, exceptionally, have found inosit, both alone and with grape sugar. It is also to be found in Bright's disease.

Some patients suffering with diabetes have a breath that smells of chloroform. The urine, odorless immediately upon being passed, after a short time also begins to smell of the same substance. Upon the addition of chloride of iron, it usually turns reddish-brown. In the distillate of such urine is found both aceton and alcohol, the result of the splitting up of ethyl-diacetic acid.

$$\underset{\text{(Ethyl-diacetic acid.)}}{C_6H_{10}O_3}+2H_2O=\underset{\text{(Aceton.)}}{C_3H_6O}+\underset{\text{(Alcohol.)}}{C_2H_6O}+CO_2+H_2O,$$

In women, 24–48 hours after ablactation and during nursing (when the milk for any reason is not withdrawn sufficiently), there appears in the urine sugar of milk.

III. Leucin and Tyrosin.

$C_6H_{13}NO_2$ and $C_9H_{11}NO_3$.

Leucin and tyrosin result from the decomposition of albumin and its nearest derivatives. They are found in great quantities in certain glandular organs of the body, when these are subjected to definite pathological changes; in the liver, the pancreas, the spleen, etc. In the urine they have been found only

in acute yellow atrophy of the liver, in several cases of phosphorus poisoning, and, in small quantities, in typhus and variola.

If these substances are present in large quantity (usually the case in acute yellow atrophy of the liver), their detection is very simple. Either we find the crystalline tyrosin in the urine, or it separates with the leucin, when the urine is concentrated in a water bath. These bodies sometimes occur in such great quantity as to partially replace urea. They are to be recognized by their characteristic microscopic forms. If they are not very abundant, and do not appear upon concentrating the urine, a large quantity of urine must be taken, precipitated with basic acetate of lead, filtered, the excess of lead removed by sulphuretted hydrogen, again filtered, and finally, the clear fluid evaporated to a small volume in the water bath. If tyrosin is present, after twenty-four hours a crystalline deposit will be observed. Leucin, which is more soluble, takes a longer time to be deposited.

Fig. 4.

a, Leucin; *b*, Tyrosin.

It is necessary to examine the urine as soon as possible after it has been voided.

The presence of leucin and tyrosin in large quantity is always an indication of great degeneration of the

proteids. Albumin is almost constantly found at the same time. Oxymandelic acid (perhaps derived from tyrosin) is frequently found in urine, and up to the present time it has never been found elsewhere.

IV. Abnormal Coloring Matter.

We must here discriminate between those substances which, being normal constituents of other fluids of the body, would, in urine, be considered abnormal, those that are found only in urine, as uroërythrin, and finally those that are entirely accidental, as the coloring matter of plants.

(*a*) Uroerythrin (Harley's Urohaematin).

In all febrile diseases the urine has more or less of a yellowish-red color (urina flammea), and the expert, in most cases, is enabled from the condition of the urine alone to diagnosticate a febrile state. This color, according to Heller, comes from the presence of uroërythrin (in addition to an increase in the normal coloring matter). When such urine has a sediment, this is red or dark red; even the clear urine, when precipitated with lead acetate, will cause a pink or flesh-colored precipitate of lead. Heller calls this red coloring matter, found in solution or in the so-called brick-dust sediment, uroërythrin.

It is said that this coloring matter contains iron; concerning its structure and origin, however, nothing definite is known. It is possible that, in diseases in which there is blood dissolution (typhus, septic fever, etc.), a part of the blood corpuscles

in retrograde metamorphosis supply material for the formation of the uroërythrin. The uroërythrin, then, could be taken as measure for the quantity of red blood corpuscles destroyed during fevers.

This coloring matter is either discovered by the presence of a brick-dust sediment, or, when in solution, by the precipitation with lead acetate above described. Only a small quantity of lead acetate in solution must be added, as it is not advisable to dilute the color in a great precipitate. If the urine contain blood coloring matter, this must be removed. The foam of urine containing much uroërythrin, may be yellow, like that of an icteric urine. In the latter, the precipitate with lead is also yellow.

The earthy phosphates, when precipitated with liquor-potassa, appear gray, while in urine containing blood-coloring matter, they are red or dichroic. The absence of albumin, the color of the earthy phosphates and the red precipitate with lead, are the points of differential diagnosis between uroërythrin and blood-coloring matter.

Uroërythrin is found in all febrile diseases, even in the mildest catarrh; it is found in greatest quantity in pyæmia, diseases of the liver and lead colic.

(β) Coloring Matter of Plants.

Many vegetable substances, especially chrysophanic acid (in rhubarb, senna, etc.), impart to alkaline urine a reddish-yellow to a deep red color. They can be recognized in that the red alkaline urine turns yellow upon the addition of an acid, but after the addition of ammonia again returns to its original red. In the test for the earthy phosphates of such an urine, they

will come down colored blood-red, so that one would be tempted to think of the presence of blood. But the earthy phosphates are never dichroic, and turn violet upon exposure to the air. The differentiation between uroërythrin and blood-coloring matter is accomplished by the lack of a response to the test for blood-coloring matter, the absence of albumin, and by the characteristic changes upon addition of acids and alkalies. It is important for the practitioner to be perfectly familiar with these tests, especially in summer, when the urine is apt to become alkaline, and its blood-red appearance be alarming without signification.

(γ) Blood Coloring Matter.

The occurrence of blood-coloring matter in urine may have a double source. Either it is derived from the kidneys, or the blood corpuscles that have been originally mixed with the urine, have been dissolved. The color of the urine varies according as hæmoglobin or methæmoglobin are present.

In hemorrhages from larger vessels the urine usually contains hæmoglobin. In parenchymatous or capillary hemorrhages the urine usually contains methæmoglobin as well, which imparts to it a reddish-brown color. The explanation why hæmoglobin should occur in one place, and methæmoglobin in the other, is probably found in the fact that in hemorrhages from the capillaries, the urine and blood are more intimately and slowly mixed, and are retained longer at the temperature of the body.

The most important factors for the change from hæmoglobin to methæmoglobin are, probably, temperature, the presence of carbonic acid, and the absence of oxygen in the urine.

For demonstrating blood-coloring matter in the urine, the hæmin test is advantageous. Precipitate the earthy phosphates in a test-tube; these will bring the blood-coloring matter down with them, and appear red. If little of the blood-coloring matter is present, they are dichroic.

If the urine is alkaline, and the test does not bring down the earthy phosphates because of their having been already removed with the sediment, we can still produce a precipitate with 1 or 2 drops of the magnesia solution, which will serve our purpose perfectly. This precipitate must be collected on a filter, then placed upon a slide, and dried carefully by means of gentle heat, when the hæmin crystals may be obtained directly from it. To this end, place a small quantity of common salt upon the dried earthy phosphates, and mix well by rubbing with a knife. Then blow the excess of common salt from the slide, place a hair upon the mixture, and after having added glacial acetic acid, cover, and heat until bubbles begin to come from under the covering glass. After cooling, hæmin crystals can be seen with the microscope. In order to avoid further decomposition of the blood-coloring matter, care must be taken to heat carefully with the liquor-potassa, and to filter rapidly. Bubbles will also develop under the cover without heating, if the slide be allowed to stand, but these are carbonic

acid gas, which must be allowed to escape, and then heat to the boiling point of glacial acetic acid. The crystals prepared in this manner are frequently small and imperfectly crystallized, but they can be easily distinguished by using higher powers.

Another method consists in making the urine alkaline with caustic soda, and adding first tannic, and afterwards acetic acid. The washed and filtered precipitate is then tested for hæmin crystals.

The crystals may be obtained, also, by coagulating the albumin, collecting this brown coagulum upon a filter, drying, and testing with alcohol which contains sulphuric acid. After the alcohol has been evaporated, the residum should be tested in the above manner for Teichman's hæmin crystals.

If we have a spectroscope at our disposal, a large test-tube should be filled with diluted urine, and placed between a lamp and the instrument, when the characteristic spectrum can be observed.

So-called hæmatinuria occurs in diseases of the general system, scorbutus, purpura, scarlatina, etc., after transfusion of blood, after inhalation of arseniuretted hydrogen—that dissolved blood-coloring matter is found in cases of true hæmatinuria, need hardly be mentioned.

(δ) Biliary Coloring Matter.

In certain conditions, biliary coloring matter, decomposed or otherwise, can be found mixed with urine. The urine contains biliprasin more frequently

than bilirubin; frequently, also, other results of oxidation of biliary coloring matter. If bilirubin is present unchanged, the proper tests will give a beautiful and characteristic play of colors; if biliprasin is present, these will produce only a green color; but if the coloring matter has been changed beyond this, the tests are negative.

For the detection of unchanged biliary coloring matter (bilirubin and biliprasin), the following tests may be used:

1. *Gmelin's Test.* Pour under icteric urine concentrated nitric acid, containing a small quantity of hyponitric acid. When the two fluids touch, the following colors in the following order will appear: green, blue, violet, red, yellow. This test can also be performed by mixing urine with dilute nitric acid, and then pouring concentrated sulphuric acid under the mixture.

2. *Heller's Test.* Pour into a small beaker 6 c. c. of pure hydrochloric acid, and then add urine, drop by drop, until the acid becomes faintly colored. Mix, and then pour pure nitric acid under the mixture. Again the play of colors will be observed when the fluids meet. If the fluids are mixed together, this play of colors will take place throughout the whole mixture. The play of colors can be especially well observed by means of transmitted light. This test is very delicate, easily executed, and sufficient for almost all cases.

To detect small quantities, it is necessary to shake 100 c. c. of urine with 10 c. c. of chloroform in a

bottle until the fluid is tinged yellow. Avoid too energetic shaking, as that will subdivide the chloroform so finely that it will no longer unite in large drops. Closing the bottle with the thumb, and lifting the latter, it is easy to allow 1 c. c. of chloroform to drop into a test-tube containing 10 c. c. of hydrochloric acid. If a small quantity of nitric acid is then added, and the whole shaken, the characteristic play of colors of Gmelin's test will be observed in the drop of chloroform. Because this play of colors takes place very slowly, and because acids act very slowly upon the coloring matter dissolved in chloroform, this test is especially valuable for the purpose of demonstration.

In all reactions for biliary coloring matter, the green color is the deciding tint. If this has not been observed, the presence of biliary coloring matter can not be deduced. Indican, for instance, will also give blue, violet and reddish-yellow, with Heller's test, but the characteristic green is wanting.

In testing for albumin with the nitric acid test, if unchanged biliary coloring matter is present, a green zone will be observed between the urine and the colorless nitric acid. If albumin is present, it is colored green by this test. Urine containing indican, may, however, even here, simulate biliary coloring matter. A blue layer is produced, which looks green by reflected light. In these cases, either perform Heller's test with the chloroform, or precipitate the urine with lead acetate, and see if it is possible to detect indican, in appreciable quantity, in the filtrate.

Ultzmann's Test. This strives to bring out the characteristic green color positively and surely. Add to

10 c. c. urine 3–4 c. c. solution of potassium hydrate (1 in 3 of water), shake, and acidulate with pure hydrochloric acid. The mixture turns emerald green.

If the earthy phosphates are precipitated from urine containing biliary coloring matter, they come down with a brown color.

When the coloring matter is so much changed that the preceding tests are negative, the following will be of service: Dip a piece of clean, white linen (or filtering paper) into the urine, and allow to dry. The linen will appear brown.

A further proof of the presence of biliary coloring matter will be found in a very dark sulphuric acid reaction. The urine does not become garnet, but black. A similar reaction will only be observed when sugar or blood-coloring matter is present. Both are to be previously excluded.

With potassium hydrate the earthy phosphates are precipitated of a brown color.

Biliary coloring matter is found in urine, independently of jaundice, in a variety of pathological changes of the liver, so that that disease can frequently be predicted several days before its appearance, from the urine. Furthermore, the biliary coloring matter is always found in phosphorus poisoning.

V. Biliary Acids.

These are rarely found in urine, and then only in small quantity. In jaundice, although the coloring matter of the bile may be present in great quantity, they are very rarely found.

In diseases of the parenchyma of the liver, accompanied by rapid destruction, they are undoubtedly found, but even then in small quantity. In such cases it must be accepted that such large quantities of the biliary acids are produced, that they can not undergo the normal changes in the blood, and are, therefore, found in the urine.

It is sometimes possible to demonstrate these acids by means of Strassburger's method: Dissolve a small quantity of cane sugar in the urine that is to be tested, dip filtering paper into it, and allow to dry. Going over this with a glass rod, dipped in sulphuric acid, which must be free from nitric acid, will produce a purple-violet stripe; red or reddish-brown is not decisive.

It is necessary, as a rule, to separate the biliary acids, in a pure state, from a large quantity of urine, and perform Pettenkofer's test.

The separation is very laborious. Evaporate about 500 c. c. of urine to dryness, in a water bath, and extract with ordinary alcohol. This solution is again evaporated, and the residuum extracted with absolute alcohol. This alcohol is again dissipated and the solid treated with water, the solution precipitated with acetate of lead, avoiding an excess; the precipitate collected, washed, and dried with filter paper. Thereupon, the salts (with lead as base, and biliary acids as acids) are extracted with boiling alcohol; sodium carbonate is added, again evaporate, and, finally, the resulting sodium salt of the biliary acid is extracted with absolute alcohol. Now permit the alcohol to evaporate, and perform Pettenkofer's test with the concentrated watery solution.

This test is based upon the fact that all watery solutions of the biliary acids, if mixed with a concentrated solu-

tion of cane sugar and concentrated sulphuric acid, will produce a violet-purple color, when they are not heated over 70° c. (158° F.). It is best to put the test-tube into cold water as soon as sulphuric acid is added, otherwise the sugar will be charred by the acid, and produce a black color.

A trace can be detected by Neubauer's modification; a few drops of the suspected fluid are evaporated to dryness on a porcelain dish, upon the water bath. A minute drop of solution of cane sugar is added (1,00 gr. sugar in 500 c. c. water), and an equally large drop of concentrated sulphuric acid. This must be heated over the water bath, until the violet color begins to appear at the circumference, when the dish should be taken from the bath, and the reaction will become more marked.

Many other substances, such as amyl alcohol, albumin, oleic acid, give the same reaction, but they can be differentiated by means of the spectroscope.

Besides the substances treated of, allantoin will appear in urine, especially after the administration of tannic acid; lactic, acetic, and butyric acids occur in cases of acid fermentation; and benzoic acid in putrid urine, as well as fats and soaps.

VI. Carbonate of Ammonium.

$$CO_3(NH_4)_2$$

All the carbonate of ammonium that occurs in urine, comes from urea, which, as has been before stated, is carbamid.

$$CO\begin{cases} NH_2 \\ NH_2 \end{cases} = \text{UREA.}$$

This is changed to ammonium carbonate by taking up water.

$$CO\begin{cases}NH_2\\ NH_2\end{cases} + {}_2H_2O = CO\begin{cases}O,NH^4\\ O,NH^4\end{cases}$$

The development of ammonium in the decomposition of urine by putridity, which may occur in the bladder, is caused by this reaction. The ferment is a body which adheres to the mucus of the bladder, and develops best during a catarrh. We, therefore, find the urine reacting alkaline in nearly all diseases of the bladder. The catarrhal secretion of the pelvis of the kidney does not seem to cause alkaline fermentation, at least, not immediately; consequently, we find the urine in pyelitis nearly always of an acid reaction. If fresh normal urine be mixed with the sediment of urine from a pyelitis, and another specimen with that of cystitis, it will be seen that the former will require between twelve and twenty-four hours to show alkalinity, while the latter will become alkaline in a very short time (two to three hours).

Ammonium carbonate is also found in the second stage of processes with exudation, so-called absorption-urine, and is considered, here, a favorable symptom. This substance can be recognized by its odor.

Urine containing it, moreover, is usually alkaline. But the alkaline reaction may depend upon a fixed alkali, as sodium carbonate, which has been taken internally. Whenever there is any doubt about the nature of the alkalinity, the following test can be used:

Put into a small Florence flask, 15 to 20 c. c. of the urine, then close the flask with a cork, perforated, in

order to allow a glass tube, of the thickness of a lead-pencil, to pass through. Into this there is put a piece of red litmus paper that has been well moistened. Heat the flask carefully in a water bath; if ammonia is present, it will be carried off with the vapor of water arising from the urine and color the litmus paper blue. Care must be taken not to boil the urine, otherwise urea will be decomposed, giving rise to ammonium carbonate.

Ammonium carbonate is found:

1. Usually in the various forms of disease of the bladder.
2. In the second stage of acute exudative processes.

According to Heller, this salt is also found in troubles of the spinal cord and grave cases of typhus, even with acid reaction of the urine.

VII. Hydrogen Di-Sulphide.

SH_2

Occasionally sulphuretted hydrogen is found in urine containing albumin, especially in troubles of the bladder, where a great quantity of pus is produced. Here it is formed from the albumin, which decomposes while in the bladder. Although the odor is characteristic, yet it sometimes becomes necessary to prove its existence by a chemical reaction. In order to do this, we use the same method employed for detecting the presence of ammonia, taking, instead of the litmus paper, a piece of filtering paper that has been dipped either into a lead or silver salt solution. The slightest amount of heat will cause the gas to escape and color the strip of paper brownish-black.

Such urine is easily detected by the fact of its coloring silver catheters black.

Accidental Constituents.

Under this heading we consider those substances that are exceptionally found or introduced into the organism, and then leave it by way of the urine.

Many substances are not changed at all in the system, as most inorganic combinations, as well as many organic (succinic acid, chloroform, quinia, carbolic acid, etc.).

Of the heavy metals, the following have been found: antimony, arsenic, copper, zinc, gold, silver, tin, lead, bismuth, and mercury; either as a result of introduction as medicine, or on account of constant handling (painters, potters, etc.).

Of the alkali salts nearly all pass into the urine; the carbonates, ammonium salts, chlorates, borates and silicates of the alkalies, ferro and ferri-cyanide of potassium, cyanide of potassium, iodide of potassium, etc. Potassium sulphide is found in the urine as sulphate. On the other hand, calcium and magnesium salts are either not found at all, or only in very small quantities.

Mineral acids (sulphuric, nitric, phosphoric, etc.) are found as corresponding alkali salts; free carbonic acid, only, appears as a simple solution in urine.

Metallic bases can be detected, either by electrolysis, or by forming an ash, and examining in the ordinary way. Arsenic is first precipitated in the ordinary way, and can then be easily detected by Marsh's method.

Many combinations, the organic ones, especially, are changed in the organism. The aromatic acids, for instance, are all excreted in the urine, as glycocol combinations; benzoic acid as hippuric acid; salicylic acid, for the most part, as salicyluric acid.

Carbonates of the alkalies are found:

1. After the internal administration of the same.
2. After the use of mineral waters.

3. After eating much fruit, because the fruit acids are all converted into carbonic acid in the system.

In these cases the reaction of the urine is alkaline. In order to prove the origin of this alkalinity, evaporate to dryness, then add a little water, and test with litmus paper. If there is an alkaline reaction, it is proof positive that there have been permanent alkali salts present in the urine.

Iodine is easily detected by adding carbon di-sulphide to the suspected urine, and then fuming nitric acid or bromine water and shaking (violet discoloration of the carbon di-sulphide or chloroform). A bluish discoloration indicates iodine. In Heller's test for albumin, iodine crystals are frequently deposited.

Salicylic acid can be detected by the violet color produced when ferric chloride is added. A similar reaction sometimes occurs in diabetic urine, even when salicylic acid is absent.

D.—Sediments.

Fermentation of Urine.

Normal urine is clear when voided. After standing for some time, the so-called nubecula is found, either at the bottom of the vessel or in the lower part of the urine; a cloud of mucus from the bladder, which is very well marked when relieved by a dark background, or when the mucus contains epithelium, an abnormally large quantity of bacteria, or traces of precipitated urates, held in suspension.

In this condition, healthy urine will keep for a long time, in a perfectly clean vessel; longer when the air is excluded—for weeks, even months. Frequently, however, a change takes place, known as acid fermentation.

Both the acid sodium phosphate and the urate of sodium are found in urine.

The phosphate acts upon the urate, by withdrawing some of its base, and changing it to an acid salt, which, being insoluble, is precipitated as a yellow or reddish powder. This reaction takes place most readily at a low temperature. At high temperatures the process of decomposition goes on. All the base (sodium) being withdrawn from the urate, and the uric acid set free, it, being comparatively insoluble, comes down in the form of a crystalline granular powder, with a brick-dust or brownish-red color, which adheres to the walls of the vessel, floats on the surface of the fluid, or rests on the bottom. Sometimes these uric acid crystals are mixed with amorphous urates, which have not, as yet, been decomposed—brick-dust sediment.

During this process no free acid is produced, as may be proved by appropriate tests.

In the greater number of instances, calcium oxalate, in small or large crystals, is mixed with this sediment.

Some of the uric acid is transformed in the body, into oxaluric acid; this, when exposed to the air for some time, changes to oxalic acid, appearing in the sediment as oxalate of lime.

This process, as will be seen, does not deserve the name, fermentation. But in some cases true fermentation, with the formation of acetic acid, takes place.

After this process has come to an end, there begins, sooner or later, another. The urine becomes paler, the crystals of uric acid have disappeared, acid reaction

gives way to neutral, which finally changes to alkaline. The urine has an ammoniacal odor, becomes very cloudy, and has a white precipitate, made up of phosphates of the earthy alkalies. Under the microscope, this cloudiness will be seen to be made up not only of suspended phosphates, but also of innumerable bacteria, at rest and also in motion. This process is actual or alkaline fermentation. The cause is the decomposition of the urea, it being acted upon by a peculiar ferment, discovered by Musculus.

Musculus recommends paper impregnated with the ferment, as a very delicate test for urea. The thick alkaline urine, which occurs in cystitis, must first be filtered. The paper used for filtering is washed with distilled water until it no longer reacts alkaline, and is then dried and colored with tumeric. Urea does not react upon turmeric, but when the ferment in the paper acts upon urea, the latter is decomposed, and the ammonium carbonate, thus generated, colors the paper brown.

NOTE.—Acid fermentation is supposed to be produced by a fermentation fungus. This fungus can be seen under the microscope, in the form of small, highly refractive, spherules. Alkaline fermentation is caused by the development of the micrococcus ureae (Pasteur). It presents itself, under the microscope, in the form of rods, which, later in their development, become cocci, looking like a string of beads. Musculus has been able to isolate a ferment from the mucus secreted by bladders affected with catarrh. An aqueous solution of this substance causes a splitting up of urea into ammonia and carbonic acid gas. As, however, the microccus ureae is present wherever there is alkaline fermentation of urine, and as it will also cause the splitting up of urea, it is fair to surmise that the micrococcus produces the ferment of Musculus, and, by means of the latter, causes the change in urea.

The ammonium may unite with the uric acid to form ammonium urate. When the formation of ammonium has reached its maximum, a part of it unites with the magnesium phosphate to form crystals of the triple phosphate. Calcium phosphate, which is soluble only in acid solutions, is precipitated, and we have the sediment of alkaline urine, composed of amorphous masses of calcium phosphate, crystals of triple phosphate, and, in the beginning, of ammonium urate.

Pus, blood or vessels already unclean with urine that has fermented, cause very rapid decomposition of the urine, it not being necessary for the urine to go through the so-called acid fermentation first.

The process is accompanied by bacteria. Various fungi can be observed upon the surface of the urine, especially in warm weather.

Classification of the Sediments.

As long as these formed constituents of urine are mixed with the urine, they cause cloudiness; as soon as they sink to the bottom, a sediment. Precipitation takes place variously; quickly in thin urine, containing heavy substances, such as uric acid or urates; slowly in albuminous, dense urine, containing light substances, such as epithelium or hyaline casts. The constituents of the sediments are either formed inside or outside of the body. The elements are either organized (occurring both in acid and alkaline urine) or unorganized, partly amorphous, partly crystalline; some found in acid, others in alkaline urine. Accordingly, the sediments can be divided as follows:

SEDIMENTS.

I, of acid urine.	II, of alkaline urine.

A.—Non-Organized.

(*a*) Amorphous.

1. Urate of sodium and potassium.	1. Calcium phosphate.
2. Fats.	2. Calcium carbonate.

(*b*) Crystallized.

1. Uric acid.	1. Ammonium urate.
2. Calcium oxalate.	2. Triple phosphate.
3. Cystin.	3. Calcium phosphate.
4. Tyrosin.	4. Magnesium phosphate.

B.—Organized.

1. Mucus and pus corpuscles.
2. Blood corpuscles.
3. Epithelium from the various parts of the urinary apparatus.
4. Casts and coagula of fibrin.
5. Spermatozoa.
6. Cancer tissue.
7. Entozoa.
8. Fungi.

They will be discussed in this order.

Non-Organized Sediments.

I. Urates.

In urine uric acid is found bound to sodium and potassium, and with them forms salts of variable structure; so that, by the withdrawal of base, more

acid salts are produced, which become less soluble, and, consequently, more ready to precipitate.

Urates are more soluble in warm than in cold water; the neutral salts are more soluble than the acid. From this, it follows, that when stronger acids are added, which displace part of the uric acid from its base, acid (less soluble) salts are produced from the neutral ones. The colder the fluid, and the smaller its quantity, the more rapidly these are precipitated. The formation of a sediment of urates is favored, then, by the following conditions:

1. Moderate addition of acid (uric acid is precipitated by a great acidity), or the action of acid salts (so-called acid fermentation).
2. Concentration of urine, either from an increase in uric acid, or by a diminution of water.
3. Cooling of the urine, which only takes place naturally after it has been voided, or in the cadaver.

The urates of the alkalies are an amorphous powder, which, on account of the coloring-matter that comes down with them, appear yellowish, grayish, brown, pink, or brick-dust red. Under the microscope they appear as small granules, grouped together like moss. If mixed with mucus, the beginner might mistake this picture for that of a finely granular cast. They can be differentiated, however, by the absence of sharp contours, by the want of plasticity, and, above all, by the reaction upon the addition of heat.

The urates disappear when warmed. Any deposit that is left, will be found to be pure uric acid. Even this disappears on the addition of an alkali and heat.

This property of the urates permits a differentiation between pus and the phosphates, without the use of the microscope. Phosphates do not occur in urine of a decidedly acid reaction. In faintly acid urine, boiling would increase the deposit, especially if potassium or sodium hydrate were added.

If the urine contains pus, boiling, alone, would not make it clearer; on the contrary, because of the coagulation of the albumin, the deposit would become denser (alkalies, however, would probably prevent this coagulation).

Finally, the murexid test, performed with the dry sediment, or the following beautiful microscopic test, would be decisive. Add to urates, which have been placed upon a slide, a drop of hydrochloric acid; after a time, crystals of uric acid will appear.

In urine that has undergone acid fermentation, and in which the alkaline fermentation has been begun, we sometimes observe crystals of uric acid, partially dissolved, but having prismatic crystals of sodium urate deposited upon them.

II. Ammonium Urate.

Acid ammonium urate is the only urate which occurs in alkaline urine, and it is, therefore, found side by side with amorphous calcium phosphate and the triple phosphate.

Ammonium urate forms brown balls, which are either developed singly, doubly, or in the form of a conglomerate, with a kidney-shaped surface. The surface of these bodies is either smooth, or covered

with small spikes, which are sometimes long, even divided, and then, most frequently, curved, producing manifold forms (Fig. 5). These forms are so characteristic that there can be no doubt concerning the nature of the crystals when viewed under the microscope.

Fig. 5.

Ammonium Urate.

Other tests are the murexid, the formation of uric acid as described above, and, finally, the addition of caustic potassa, producing bubbles of liberated ammonium.

III. Uric Acid.

The occurrence of uric acid is due, partly, to the same causes that have been discussed under the head of urates. Normally, crystals of uric acid are found at the termination of so-called acid fermentation, in concentrated urine, especially in summer, where high temperature prevents the deposit of urates; then, in pathologically increased formation of uric acid, in which case neither water nor alkalies suffice to keep the acid in solution.

The primary form of uric acid is that of rhombic plates with rounded, blunt corners.

This form is known as the whetstone. The crystals may be very small or developed singly. Sometimes they group about foreign bodies, as threads, hairs, and then form cast-like bodies. At other times the individual crystals are highly developed and collected together, appearing either fan-shaped or like shingles upon a roof. Besides this, barrel-shaped, and, in other cases, lance-shaped crystals, frequently united to form rosettes, are found. The rough and lance-shape forms are of great practical importance, as they always have some connection with the formation of calculi in the kidney. They only occur in very acid urine. When this is counteracted by the internal administration of fixed alkalies, the form of the crystal changes to the normal, that of the whetstone. These forms are frequently found in the sediment of pyelitis calculosa, and also accompany albuminuria (hyperæmia of the kidneys) and hæmaturia. Intense desire to pass

Fig. 6.

URIC ACID.—*a*, Rosette; *b*, Whetstone; *c*, Dumb-bell; *d*, Barrel-shaped; *e*, Lance-shaped.

water, without albuminuria or pyelitis, is occasionally found in patients whose urine contains these forms.

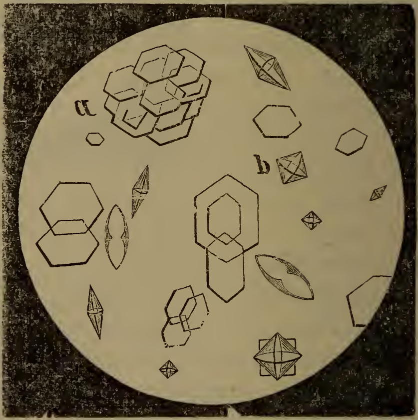
In all cases the uric acid appears colored; faintly yellow, brownish red or dark brown, on account of coloring matters which are brought down with it.

The crystals are usually so well developed that they appear like glistening brick-dust red sand upon the bottom of the vessel, and may be diagnosticated with the naked eye. This sediment is dissolved in caustic alkalies.

IV. Calcium Oxalate.

Oxalic acid has great affinity for calcium. As there is calcium in urine, the oxalic acid formed in the kidney, or in the urine, must be found in the latter in the form of calcium oxalate.

Fig. 7.



Calcium Oxalate and Cystin.—*a*, Cystin; *b*, Calcium Oxalate.

These crystals, as has been stated, frequently appear with uric acid during acid fermentation. The crystals of calcium-oxalate are of a very characteristic shape. They are flat octahedra, which refract the light very much; sometimes having

the appearance of small points, sometimes of squares, whose corners are connected by diagonals, which make them look like envelopes. (See Fig. 7.) Besides this form, there is also that of the hour glass (dumb-bell). These crystals easily escape detection by the inexperiened, on account of their low specific gravity, which causes them to be very slowly deposited. The urine must be allowed to stand from twelve to twenty-four hours, to allow them to settle.

The characteristic form of these crystals prevents error in diagnosis. The only crystal which could be mistaken for them is the triple phosphate, but that is always larger than the calcium oxalate, and is always found in neutral or alkaline urine, whilst the calcium oxalate is only present in an acid urine. And, finally, acetic acid dissolves the triple phosphate, and not the calcium oxalate.

V. Cystin.

Cystin forms regular hexagonal plates, varying in size, and arranged either singly, or with one or more smaller crystals lying upon a larger one. Sometimes a large crystalline plate shows cleavage corresponding to the outline of a hexagon. Twin crystals are of rare occurrence, and small, poorly developed crystals are collected together in irregular masses. (See Fig. 7.)

Sometimes the corners of the crystals are rounded, as if they had been melted off. The crystals are always colorless, and can only be mistaken for an exceedingly rare form of colorless uric acid. This latter

possibility might arise if dissolved cystin had been precipitated from the urine by acetic acid, producing a similar, but more irregular deposit of uric acid, in hexagonal plates, hardly as regularly formed as those of cystin.

In order to prove whether the crystal under the microscope is cystin, allow a drop of ammonia to flow under the thin cover; with this treatment cystin would immediately disappear, whilst uric acid would remain, unless heated. As soon as the ammonia has evaporated, the cystin crystallizes again; this process may be hastened by adding a drop of acetic acid to the ammoniacal solution.

A second test consists in adding a drop of hydrochloric or oxalic acid to the crystals. This dissolves cystin, while uric acid remains unchanged. It can not be mistaken for the urates on account of its form, and because it is entirely insoluble in warm water.

As cystin is soluble in ammonia, but not in ammonium carbonate, alkaline fermentation precipitates it as it does the earthy phosphates. From these it can be differentiated both by microscopic and chemical tests.

Acetic acid dissolves the earthy phosphates, but leaves the cystin unchanged. When this mixture is boiled, the greater part of the sediment sometimes dissolves, and the remnant may reveal hexagonal plates, under the microscope, which must be tested with ammonia and hydrochloric acid, in order to separate the cystin from the uric acid which may be present.

Cystin which has been dissolved in liquor potassa, heated, and mixed first with water and then a solution of sodium nitro-prusside, will turn violet, (sulphur reaction).

Urine containing cystin is usually pale; upon decomposition the odor of sulphur, besides that of ammonia, is developed; this is probably because of the presence of sulphur in cystin. The sediment is found in company with a cystin calculus, and also alone. It appears white, or grayish, mixed with triple phosphates and calcium phosphate, and in acid urine with calcium oxalate.

With us this sediment is very rare, but it is said that cystinuria has frequently been observed in several members of the same family.

VI. Leucin and Tyrosin.

(See Fig. 4, Abnormal Constituents.)

Leucin appears under the microscope in the form of more or less colored spheres, of various sizes, which resemble fat globules. Their contours are sharp, and with a good light they show radii and delicate concentric lines.

Tyrosin forms very fine, short needles, which cross each other and collect in groups, which lie upon each other in such a way as to form crosses. Sometimes it is found as a sediment, but more commonly we find globules of leucin mixed with it.

Mistakes between leucin and fat globules can be avoided by testing with ether, in which fat is soluble,

and leucin, insoluble. The crystals also dissolve in potassium hydrate, but not in cold mineral acids.

Tyrosin crystals can be verified in two ways; by Piria's and by Hoffman's test. The first method consists of putting a small quantity of sediment into a watch glass and moistening it with two or three drops of concentrated sulphuric acid; this must stand twenty or thirty minutes, when water is first added, and then calcium carbonate, until effervescence ceases, after which the whole must be filtered. If, on the addition of ferric-chloride (free from acid), a violet discoloration takes place, the sediment is tyrosin.

The second method is simpler. Pour water over the sediment, and boil. To the boiling fluid, add a drop of a solution of mercuric nitrate. A red precipitate is formed, and the fluid changes to pink or purple.

Leucin and tyrosin are seldom found in urine, and when they do occur, it is nearly always in cases of acute yellow atrophy of the liver, or in phosphorus poisoning.

VII. Fat.

One must be very careful not to consider the film of fat which is found upon urine, as a product of the urinary organs. We can satisfy ourselves in every case, that it is the result of the introduction of the catheter. We must be equally cautious in regard to finely divided drops under the microscope. They are usually the result of some foreign admixture, as oil in the vessels in which the urine has been preserved; fat upon the slide, milk, etc.

The statement that a high degree of fatty degeneration in the kidney will produce fat globules in the urine, is one which, as a result of observation, we can not confirm. *A priori* this is not probable, on account of the fact that that part of the kidney which is fatty does not excrete urine; this view also requires the assumption that the fat is separated from the kidney in the form of drops. That this is not the case, can be shown upon the post-mortem table.

Emulsified fat is found in the chylous urine of the tropics, whose turbidity, inasmuch as it depends upon fat, can be made to disappear readily by ether. It never forms a sediment, but, on account of its low specific gravity, is found, like cream, upon the surface of the urine.

Under the microscope, fat shows globules with very sharp outlines, which ether dissolves.

Cholestearin is found simultaneously with the fats; this occurs rarely, however, and then only in its crystalline form. It is recognized by its characteristic crystal form, transparent rhombic plates.

Galacturia is very rarely met with in temperate climates.

VIII. Earthy Phosphates.

(a) *Amorphous.*

A layer of grayish-white sediment is frequently found in ammoniacal urine, which the beginner might mistake for pus; it consists of the precipitated earthy phosphates, *i. e.*, calcium and magnesium phosphates.

As has been stated, these salts are only soluble in acid fluids; they, therefore, precipitate as soon as the urea is split up, causing alkalinity of the urine.

The earthy phosphates appear, under the microscope, like granules of varying size, unlike the urates, however, in configuration. Differentiation can easily be effected by chemical tests.

The urates, with the exception of ammonium urate, occur in acid urine, whilst the earthy phosphates, excepting the crystallized calcium phosphate, are only found in alkaline urine. The litmus reaction is thus sufficient to solve the question of urates or phosphates. An addition of sodium or potassium hydrate will dissolve the urates, whilst phosphates will remain unchanged.

Differentiation between pus and the phosphates will be discussed further on.

All causes for alkalinity of urine produce this sediment, which varies according to the quantity of earthy phosphates originally held in solution by the urine.

In exceptional cases, in diseases of the bladder, and when great quantities of alkalies are taken internally, the urine is passed alkaline in reaction. When this occurs, it is turbid, because the precipitation of the phosphates had taken place in the bladder; as a rule, precipitation takes place after the urine has been passed.

The so-called triple phosphate, in its characteristic form, is always mixed with the earthy phosphates in the sediment.

(b) *Crystallized Calcium Phosphate.*

This substance ($PO_4HCa+2H_2O$) is found in pale, faintly acid urine which has a tendency to alkaline fermentation, and is usually very rich in calcium phosphate.

The sediment seems to occur as a result of individual predisposition. Persons, otherwise perfectly healthy, are observed, whose urine always contains this sediment in summer.

Under the microscope, either single, wedge-shaped crystals are found, or various arrangements of them; several of them lying together, or having their apices directed towards one point, or in the form of rosettes, with the bases of the crystals forming the periphery of the rosette. The form of the crystal is so characteristic that error is hardly possible.

The triple phosphate never forms rosettes, and uric acid can always be distinguished by its color and insolubility in acetic acid.

IX. Magnesium Phosphate.

In neutral or faintly alkaline urine, long quadrilateral plates, with rounded ends [basic magnesium phosphate (probably $Mg_3(PO_4)_2+17H_2O$)] are occasionally observed. Especially is this the case after the internal administration of carbonates, or mineral water containing them. If a drop of a solution of ammonium carbonate (in five parts of water) is added, these plates become opaque and rough, and their

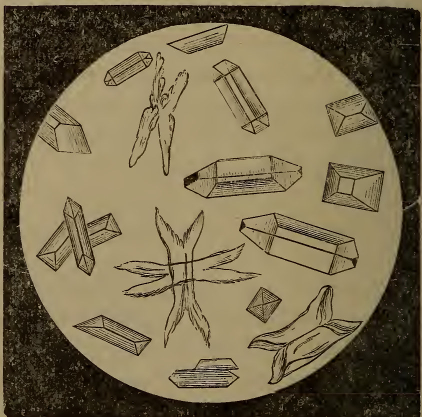
corners fade. Calcium phosphate is affected much more slowly, and does not become opaque, and the triple phosphate shows no change, whatever, with this test.

This sediment is very rare, and can only develop in highly concentrated urine which was originally of a neutral or alkaline reaction. If the alkalinity is caused by alkaline reaction, no magnesium phosphate can be formed, ammonium magnesium-phosphate being the invariable result.

X. Triple Phosphate.

This substance is immediately recognized by its large, transparent crystals, which refract the light very much, and have well-developed surfaces and angles. Among the many combinations of the rhombic form, hemimorphous, the coffin lid, is frequently best known. The only conceivable mistake to be made, is between common salt, calcium oxalate, and this crystal. Common salt is never found in natural urine,

Fig. 8.



Triple Phosphate.

only in that which has been concentrated by evaporation. The reaction with acetic acid prevents any error in diagnosis regarding the larger crystals of calcium oxalate; the triple phosphate always disappears upon the addition of this reagent. The conditions producing the appearance of triple phosphate are the same as those discussed under the head of earthy phosphates.

XI. Calcium Carbonate.

Urine of most of the herbivora is turbid when voided, depending upon the separation of calcium carbonate. This condition is only exceptionally found in the human being, where the sediment usually forms some time after the urine has been passed.

The causes for this phenomenon are obscure.

It is probable that the sediment never occurs alone, but that it is mixed with earthy phosphates. It commonly forms a coarsely granular or fine powder; occasionally it forms dumb-bell crystals; this, however, is exceptional. It is recognized by its effervescence and solubility upon the addition of mineral acids, which can be observed under the microscope.

If a drop of hydrochloric acid is allowed to flow under the covering glass, small bubbles of gas (carbonic acid gas) will be seen to escape. This never occurs when earthy phosphates alone are present. Before making this test, the sediment must be carefully washed on a filter, to remove the ammonium carbonate, which would show the same reaction as the substance tested for.

Organized Sediments.

I. Mucus.

Great quantities of mucus may be present in urine without being easily detected, on account of the similarity that exists between its index of refraction, and that of urine. Mucus can only be seen in the form of the nubecula already described, after the urine has been allowed to stand for some time; when a great and rapid development of bacteria has taken place, and when an abnormally great quantity of epithelium is present. When these conditions are not present, it is necessary to color the urine.

If albumin is absent, the mucus can be precipitated by alcohol which has tincture of iodine in it, or by acetic acid to which a solution of iodine in potassium iodide has been added. Acetic acid produces a turbidity in solutions of mucin, which is not dissolved by excess of acid, but which disappears when a few drops of hydrochloric acid are added. If the turbidity disappears upon heating, it was due to the urates, and not to mucus.

Mucus does not show any characteristic appearance under the microscope, but small bodies are found suspended in it; crystals of oxalate of lime and uric acid, mucus corpuscles (young cells), or epithelial cells of the bladder. Mucus which has been coagulated by acetic acid shows a finely granular, striped mass, which sometimes resembles casts.

In women the nubecula is usually larger than in

men, because more or less mucus is always present, from the vagina, especially in leucorrhœa.

As mucin swells up, instead of dissolving, in water, it can be separated from the urine by filtration. It remains on the filter, and when dry looks like a varnish.

Urine which contains much mucus is not easily filtered, because the mucus fills up the pores of the paper.

II. Epithelium.

Besides the mucus corpuscles which are found suspended in mucus, we also find in urine, cells of another description; cells which formerly lined the urinary apparatus, or formed part of the glandular substance of the kidneys. The forms of these cells are less manifold when in urine than when taken directly from the organs of the cadaver, because the urine alters their shape.

The forms of the cells may be divided into three classes:

1. Round cells.
2. Conical cells and cells with processes.
3. Flat cells.

1. The round cells come from the uriniferous tubules and the deeper layers of the membrane lining the pelvis of the kidney. In the beginning, they are more or less flattened, depending upon the manner in which they were originally arranged. Influenced by the urine, they swell up and represent spheres. They have a well-developed nucleus, and by it are differ-

Fig. 9.

a, Epithelia from male urethra; *b*, from the vagina; *c*, from the prostate gland; *d*, from Cowper's glands; *e*, from Littré's glands; *f*, from the female urethra; *g*, from the bladder.

entiated from pus, whose cells are granular, and only show a nucleus upon the addition of acetic acid. Epithelial cells have but one nucleus, pus cells have two or three, rarely more, and epithelial cells are the larger.

In acid urine, epithelial cells are preserved for some time, but when the urine becomes neutral or alkaline they appear larger, nearly hyaline (the granular protoplasm collecting around the excentric nucleus), and are finally completely dissolved.

The epithelium of the male urethra can not be easily distinguished from that of the kidney, by the microscope. The chemical reaction of the urine must here be taken into consideration. If the urine contains albumin, the cells originate in desquamation in the uriniferous tubules; this not being present, the cells are, in all probability, from the urethra.

Cells from the prostate, Cowper's and Littré's glands, are like those of the urethra, and can not be distinguished from them by means of the microscope; in all

probability they occur rarely in the urine. Fused with mucus and pus, they form the shreds found in gonorrhœa.

The conical cells and cells with processes, in the majority of cases, come from the pelvis of the kidney; very fine and delicate cylindrical cells may be from the accessory organs of the male urinary apparatus, but these are quite rare. They are commonly twice as long as they are broad, and tapering towards one extremity. The second variety may have either one or two processes (unipolar and bipolar cells). The occurrence of these must not be considered as a symptom of noeplasmata, as is laid down in many of the older text books.

3. Flat cells either originate in the bladder or in the vagina.

As the name indicates, their form is flattened. Usually, they are irregular, polygonal, having rounded edges and a dark, sharply-defined nucleus, which is nearly central. The latter protrudes somewhat, and a cell of this sort, when seen in profile, appears thicker in the middle, like a spindle-shaped cell.

It is only with difficulty that epithelium of the bladder can always be distinguished from epithelium of the vagina. The cells from the bladder are more delicate, and usually are found singly; those from the vagina are tougher — sometimes seem like scales; nearly always in larger or smaller flakes, above all, in layers, something which can not occur with epithelium of the bladder.

Yellow discoloration of the nuclei of various epi-

thelial cells in jaundice, is of interest. If a drop of fuming nitric acid is allowed to flow slowly under the thin covering glass, the well-known play of colors of Gmelin's test (green, blue, violet,) is produced (Ultzmann).

III. Pus Corpuscles.

Pus corpuscles in urine have the same microscopical characteristics that are possessed by those from a suppurating wound. They are round cells, twice the size of red blood corpuscles, and have a granular exterior, which covers over, and hides, the nuclei which will immediately appear, however, on the addition of acetic acid. The granular appearance will then disappear, the corpuscles swell, and the multiple central nuclei become visible.

One form, more rarely found, differs from these; its corpuscles, instead of being round, have many processes, and resemble the amocba.

Pus corpuscles undergo especial changes in alkaline urine; these are due to the action of ammonium carbonate, which fuses, melts them together, when the microscope reveals an homogeneous mass with nuclei. Such pus forms an adherent, vitreous mass, which can only be poured out, as a whole, somewhat like the white of egg.

Especial attention must be called to the fact that these masses are neither albumin nor mucus. The former *never* forms a sediment, and the latter *never* forms adherent masses. When pus is present, pus-serum must also be, and, therefore, albumin. In

every case, then, the albumin test discovers albumin, which is not the case with mucus.

The number of pus corpuscles varies very much. In some urine so few are found that they are not detected by the naked eye; in others, they are so numerous that a yellowish or grayish-white precipitate of the height of a finger is found.

In acid urine it is possible to confound the urates with pus; in alkaline, the phosphates. The former have already been differentiated in another place. The phosphates disappear upon the addition of a few drops of acetic acid, pus does not.

But we have a positive test, without using the microscope, for pus—Donné's.

Pour the urine from the sediment; add to the latter a piece of caustic potassa or soda, and stir with a glass rod. If the sediment consists of pus it will lose its white color, will become green and vitreous, denser and, finally, be reduced to an adherent mass, *i. e.*, it assumes the appearance of pus in ammoniacal urine. As there exists in urine no other body which produces this reaction, the test is a positive one, only that when the quantity is small, the sediment will disappear, and in its stead a mucilaginous fluid will appear, but no mass.

We not infrequently find in the sediment pus corpuscles which have been destroyed (detritus), blood corpuscles, epithelium, etc.

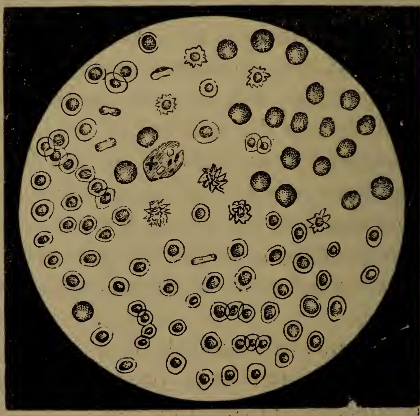
IV. Blood Corpuscles.

The presence of blood corpuscles, even in small numbers, can easily be detected by the microscope.

When urine, which is suspected of containing blood-coloring matter, or blood corpuscles, appears of a brownish-red tint, it must be allowed to stand for some time in order to permit the light corpuscles to come down as a beautiful red sediment (frequently only a trace).

In acid urine, the corpuscles retain their shape a long time, represented by small discs possessing shading which corresponds to a central depression. If seen in profile they appear bi-concave. They are always separate (except in excessive hemorrhage from the bladder), when they are arranged in money-roll order and appear reddish, slightly tinted with green. This original form is subjected to many changes, according to the fluid in which the blood corpuscles are found. If the

Fig. 10.



Blood Corpuscles.—To the right and above—red corpuscles acted upon by diluted urine; to the left, acted upon by salts; in the middle, the crenate form; and below, the normal.

urine is very much diluted, especially when beginning to be alkaline, they swell up. The depression disappears, the blood corpuscle becomes spherical and seems smaller than before. The shading in the center disappears with the depression, but appears at the periphery, by which it is recognized as a sphere.

When acted upon further, the corpuscle becomes less distinct, appears as a small bubble, then as a mere shadow. and, finally, disappears altogether.

By the action of salts, blood corpuscles become smaller and crenate. The latter form is sometimes found in urine, by the side of the normal. They seem to be produced by small crystals whose corners lift up the surface of the blood corpuscle. Instead of being round, the corpuscles are sometimes oval, varying in size, and twisted into the form of a cup.

In haematuria, accompanying parenchymatous diseases of the kidney and bladder, we almost always find spherical corpuscles of varying size. Very small, even dust-form corpuscles (mycrocytes) are found in these cases by the side of normal and large forms (macrocytes).

When blood corpuscles are present, even in very small quantity, albumin can always be detected.

If the corpuscles are dissolved by alkaline urine, the blood-coloring matter (haemo-and methaemo-globin) can be detected by methods elsewhere described.

The etiology of bloody urine will be discussed in Chapter VIII.

V. Casts.

These structures are of the greatest importance for the diagnosis of kidney disease; because of their form, which discloses their origin—the uriniferous tubules—they are called casts.

In searching for them, great caution must be observed to avoid overlooking them. Their low specific gravity causes them to remain long-suspended in the urine, and, further, they only appear in urine which contains albumin, in which all suspended matter will settle slowly.

The urine must first be allowed to stand for several hours, then carefully decanted, and the remainder poured into a wine-glass and allowed to stand for one or two hours. The last drops of the sediment are put under the microscope for examination.

One must not be satisfied with one preparation, as it is frequently necessary to examine several, otherwise the casts elude discovery. On the other hand, one must guard against mistaking other structures for casts. Beginners are apt to consider every cylindrical arrangement of phosphates or urates, especially when deposited in mucus, as finely granular casts.

Casts are usually accompanied by albuminaria, but just as we find cases in which albumin exists without the casts, so do we find casts without albumin.

Examples of the first anomaly are found in albuminuria of interstitial nephritis, in the amyloid and the hyperaemic kidney; the latter may occur in any serious inflammatory process, in which the casts may

precede the presence of albumin by from twelve to twenty-four hours.

Amongst the many varieties of casts, the following may be considered typical forms: 1, the coarse fibrin cast; 2, the finely granular cast; 3, the hyaline cast; 4, the epithelial cast; 5, the so-called uric acid cast; 6, casts of bacteria and cocci.

1. *Coarse Fibrin Casts* are roller-like, coarse, frequently corkscrew coagula, with sharp outlines, and of yellowish or brownish-yellow color. Their diameter, greater than that of any other cast, indicates that they are formed in the lowest part of the collecting tubule, near its opening into the papilla. Not infrequently epithelial cells adhere to them. Bloody casts may be considered as a variety of this form, consisting of coagulated blood from rupture of the glomeruli. They are always dark brown, and, in some cases, seem to consist entirely of blood corpuscles; in other cases, we observe in one part of the cast coagulated fibrin only, and in the other, only blood corpuscles. This form is

Fig. 11.

CASTS.—*a*, Finely granular; *b*, waxy; *c*, blood-casts.

always accompanied by blood corpuscles in the sediment. (See Fig. 11, *c*).

2. *Finely Granular Casts* (Fig. 11, *a*) are more delicate than those described above. They, apparently, are derived from the smaller tubules. They possess distinct contours, and, as their name implies, are finely granular throughout their whole extent. They are straight and tapering, either at one or both ends. Their diameter is the same throughout, narrowed at one point. In their granular structure, also, many modifications are observed. In places they are coarsely granular, in others this appearance is nearly lost so that they approach the hyaline casts, to be described presently (half-granular casts). Sometimes distinct fat globules are present. The addition of acetic acid, in some cases, causes a decided clearing up; in others, no effect at all is produced. The color of these casts is a faint grayish yellow.

Both forms retain their shape for a long time in acid urine, losing it gradually in alkaline urine.

3. *The Hyaline Cast* (Fig. 12, *b*) is partly of the size of the granular casts, partly, much smaller. They are either perfectly straight, frequently of considerable length, or curved. Whilst some give the impression of a solid, others seem like tubes with very delicate walls; the one being decidedly cylindrical, the other, tape-like.

Spiral casts, with one or more turns, are not infrequently found. With the larger of these, distinct outlines can be traced, but the smaller ones look shadowy under the microscope, and can only be separated from

their surroundings with difficulty. In such cases, it is advisable to add a few drops of a solution of iodine in iodine of potassium or aniline violet, to bring out the outlines. This causes the casts to turn yellowish (or bluish-violet), when they can be easily distinguished. They show no signs of granulation, but are pellucid and hyaline.

Fig. 12.

CASTS.—*a*, Uric-acid casts; *b*, hyaline; *c*, epithelial cast.

The size of the tape-like casts justifies us in the conclusion that they originate in the finest ramifications of the uriniferous tubules, perhaps, from the ascending limb of Henle's loop.

Hyaline casts disappear very rapidly in alkaline urine.

4. *Waxy Casts* (Fig. 11, *b*) are generally of the same breadth as the granular casts; they are perfectly vitreous, refracting light to such an extent that their outlines stand out somewhat like crystals of the triple phosphate, or similar clear crystals. They are straight, with sharply-broken, or tortuous ends. Their surface is sometimes wavy, as if the cast were made up of masses of colloid substance, which had become

fused. In places a distinct cleavage is noticeable, which gives the impression of a gelatinous mass, which had been compressed and has given away. They show the amyloid reaction, and possess greater resistance than other casts. This form is very rare, and has been found only in amyloid degeneration and tuberculosis of the kidney.

5. *Epithelial Tubes and Casts* (Fig. 12, *c*).—There are processes in which the epithelial lining is stripped, in toto, from the membrana propria of the tubules, and is washed out of them on account of the *vis a tergo* of the urine, or of a fluid exudation.

Such casts, made up of epithelial cells, are hollow, and are called tubes.

Casts, covered with epithelial cells, as with the finger of a glove, are found in the same sediment, from which the hollow tubes may be absent. These cells are always cloudy, somewhat swollen, and are rarely possessed of sharp outlines. They are frequently so much enlarged as to look more like a finely-granular mass, but the nuclei, which are present at regular intervals, betray the cell formation.

Amongst epithelial casts some are found, in which the epithelial layer is wanting in places, and the congealed exudation can be seen; and others, in which the central exudation protrudes beyond the epithelium.

6. *Uric Acid Casts* (Fig. 12, *a*) differ greatly from the preceding ones, as regards structure, and can be classed with them, only because of their common origin. They are most commonly found during the first days

of life in children suffering from uric acid infarction. Small red bodies can be observed in the urine, as well as in the liver, of such patients, which show a cylindrical structure under the microscope. They are not made up of pure uric acid, as the name would lead us to suppose, but balls of urates. In color they are brownish-red; in structure, decidedly granular, and in size they vary greatly. Treated with potassium hydrate, ammonia escapes, and the casts disappear. Parts of casts are also found.

7. *Casts* made up of *Bacteria* and *Cocci* occur only in suppurating interstitial nephritis, and not then, unless the disease is complicated with emboli of bacteria in the uriniferous tubules (Nephritis Parasitica—Klebs).

These casts are similar to the large fibrin casts in shape and size. They come from the collecting tubules, and are sometimes dichotomously divided, showing that they originate where two large tubes unite. They are made up entirely of cocci and bacteria. On account of the bacteria being at perfect rest, the casts resemble the coarse granular ones, but high powers make mistake impossible.

Several forms mentioned in other text-books are not given here; because having failed to observe them ourselves, we conclude that they must be exceedingly rare. We refer here to casts of pus cells, which must not be mistaken for those short plugs which close up the mouths of tubules at the papilla, and are characteristic of chronic pyelitis; furthermore, casts, composed of calcium oxalate, and casts that have uric acid imbedded in them. It is very common to find casts

that have calcium oxalate or uric acid adhering to them, but these are not imbedded in the cast, and have, consequently, been accumulated outside of the uriniferous tubule.

IX. Fungi.

Fungi, in different stages of development, are found in urine; some are frequently met with, whilst others are merely accidental admixtures.

The forms which are most commonly seen are: 1. Bacteria. 2. Yeast Fungus. 3. Sarcinae. 4. Oïdium lactis. 5. Spores and fragments of penicillium glaucum.

1. *Bacteria* are found principally in alkaline urine. Writers have differed as to their character, some classifying them as vegetables, others considering them animals; hence the difference in their names—vibriones, monas crepusculum, microzyma, etc. It now seems settled that they must be considered as fungi belonging to Nageli's schyzomycetes. They vary so much in appearance, that it seems practical to give different names to the different forms, according to A. Vogel, but it must always be borne in mind that it is merely different forms of one and the same fungus.

(*a*) *The Monad.*—Round, punctiform bacteria, either at rest or vibrating. Care must be taken not to take earthy phosphates having molecular motion for these fungi. Granules of a dead body have motion, but do not change their place in the field like the bacteria.

(*b*) *The Rod.*—Very small rods, hardly as long as

the diameter of a red blood corpuscle, whose thickness is too small for measurement. Both extremities are somewhat dilated. They are at rest or in motion.

(*c*) *The Leptothrix, or Chain Form*, are long chains, frequently extending over the whole field, and can be distinguished from vibriones by their length. With high powers their structure can be observed. They rarely move, and then very slowly.

(*b*) *The Vibrio*, originating in the former. Several rod-bacteria adhere to each other, and either move in a spiral direction, or the members at the ends vibrate like the tail of a fish. They frequently move with great rapidity.

(*e*) *The Zooglea Form.*—Masses of punctiform bacteria, held together by a gelatinous mass, and looking like a mass of earthy phosphates imbedded in mucus.

All these forms can be observed in one urine, even in one preparation.

Fig. 13.

FUNGI.—*a*, Micrococci and vibriones; *b*, Sarcinae; *c*, Saccharomyces urinae; *d*, Yeast-fungus; *e*, Penicillium glaucum.

2. *The Yeast Fungus—Saccharomyces Urinae.*—Single, vesicular cells of the size of red corpuscles, somewhat oval. Commonly arranged in a beaded form, or as one large cell

having several smaller ones resting upon it. Their number is usually much smaller than that of bacteria; they are found principally in acid urine, and in warm weather this fungus is very like the yeast fungus of beer (saccharomyces cerevisiae), without being identical with it. In the urine of diabetes, the same form, better developed, is found.

3. *Sarcina.*—This fungus resembles the sarcina ventriculi, but is much smaller. It is arranged in groups of two, four, eight, etc., cells, which look very much like bales of goods, where they are collected in the form of cubes.

Urine which contains this form of fungus is usually alkaline, consequently, calcium phosphate and the triple phosphate are found in connection with it. The sarcinae usually appear for weeks, even for months, in the urine of the same patient.

4. *Oïdium Lactis.*—Long cells, to be recognized by their nuclei placed in rows at regular intervals. This form is not uncommon in fermenting diabetic urine. Besides the forms already mentioned, we find in urine sporules of

5. *Penicillium Glaucum*, partly engaged in segmentation. They are sometimes mixed with fine urates, which causes them to appear brownish-red, and fur-like; or where they have developed further, we find a network of fine thallus threads.

The seeds for the development of these forms, as a rule, are mixed with the urine outside of the bladder. Like other rules, this has its exceptions. The sarcina is voided with the urine; this is also the case, some-

times, with bacteria, but the cause is to be found in unclean catheters and sounds. We have rarely met with cases of bacteria in the urine in which an instrument had not been introduced into the urethra or bladder.

Whether these structures play a rôle in fermentation and the reaction of urine, is very doubtful. The small chains appear, not only in alkaline urine, but wherever albuminous substances undergo decomposition. We find them, therefore, in secretions from a variety of ulcers, in bad pus, in passages from cholera patients, etc.

A membrane named kyesteïne, made up of fungi, calcium phosphate, triple phosphates, and sometimes animal organisms, was formerly held to be characteristic of the urine of pregnant women. This, being also found upon the urine of males, is of no value as a sign of pregnancy.

VI. Spermatozoa.

Spermatozoa, when viewed with a high power, have the appearance of small spherical structures, with a hair-like tail. In urine, they are seldom found in motion. Urine containing sperm frequently shows small, cloud-like bodies, which, under the microscope, are seen to consist of spermatozoa imbedded in a finely granular mass. The spermatozoa are very light, and therefore require from six to twelve hours before they are found in the sediment. They may be found

several days after the urine has been passed, and under the following conditions:

1. After coitus, nocturnal emissions, etc., when semen has remained in the urethra, and been washed out by the urine.

2. Spermatorrhœa; in grave attacks of typhus, involuntary passages of semen have been observed.

Spermatozoa are found in the urine of women after coitus, and may be of medico-legal importance.

VII. Histological Elements of Cancer.

Two forms of cancer elements are observed, both very rarely, however. (*a*) *Single cancer cells;* (*b*) *Pieces of cancer tissue.* (*a*) The cells vary; frequently of uncommon shape, large, caudate, with multiple nuclei. So-called nests are sometimes met with. We must avoid mistaking caudate cells from the kidney (pelvis) for cancer cells. The cells correspond to the epithelial covering of the cancer granulations, and commonly origi-

Fig. 14.

Cancer Tissue and Cells.

nate in the bladder. We are justified in making a probable diagnosis only when these peculiar cells are present in great quantity.

(*b*) *The Stroma of the Papillary Cancer* occurs in various forms in the sediment. Either it is well preserved, which occurs rarely, and makes the diagnosis easy, or it is necrotic, when the diagnosis of these papillary proliferations is exceedingly difficult.

When well preserved, the villous tissue presents, in its finest sub-divisions, dentritic structures resembling fingers, easily studied with a power of three hundred diameters. These consist in an ecstatic blood-vessel, which is usually covered by one layer, only, of epithelium. This, however, is a rare picture, and the dead modified papillæ are more commonly found, whose diagnosis is exceedingly difficult. In these, the dentritic form can no longer be verified, the epithelial covering has been destroyed, and the papilla, itself, infiltrated with pus corpuscles. In this formless mass, however, structures are occasionally found that make the diagnosis much easier. They are:

Beautiful crystals of hæmatoidin, when the necrotic tissue is treated with glycerine. They are of a yellowish-brown color, and appear either in the form of rhombs or bundles. Under the microscope, this tissue gives the characteristic reaction for bile coloring matter, when treated with fuming nitric acid. Hæmatoidin only occurs in old extravasations of blood; it is never found in urine as a sediment in its isolated crystalline form. But if we find these crystals imbedded in necrotic tissue, the diagnosis of old

necrotic and hemorrhagic tissue is a positive one, and this latter has been found only in papillary tumor of the bladder. The hæmatoidin villus can be found only in acid urine.

Another form of crystal, which we have found only in necrotic cancer tissue, and only in acid urine, is a rare form of calcium oxalate, small, colorless, aggregated, flaky crystals, in the form of dumb-bells crossing each other, and sometimes presenting a spherical form.

With low powers, we occasionally find in one of these flocculi, dense, dark, tubular, branched structures. These are the minute blood-vessels, which are still to be seen in the villus.

When the urine is highly alkaline, the papillæ may be covered with phosphates, and so changed that a diagnosis is next to impossible. One examination does not suffice for a recognition of this disease.

VIII. Entozoa.

Thus far, we have never found parts of entozoa in urine. According to other authors, the hooklets of echinococci occur in the sediment. We have, however, observed hooklets, as well as a piece of an echinococcus-sac with the animals, in fluid drawn from a tumor of the kidney, and it is possible that hooklets are found in the urine when such a tumor breaks into the pelvis of the kidney.

Hæmaturia, produced by entozoa, is frequently observed in the tropics. The entozoon which has the

most importance in this respect, is the distoma hæmatobium, or the bilharzia hæmatobia, which probably migrates from the intestine into the venous plexus of the prostate gland, where it lays its eggs. These are of oval form, with a sting-like process at one end. They plug up the smaller vessels of the bladder, catarrh with hemorrhage is produced, and the eggs are discharged with the urine.

The fact that a great many accidental impurities, which have no relation to the urinary apparatus, may be found in urine, is hardly worth mentioning; pieces of feathers, of wood-cells, of plant parenchyma (tobacco leaves, for instance), dust, very fine fibres of cotton, silk, etc. Neither is it necessary to mention that care must be taken to avoid mistaking substances on the slide or its thin cover, or air bubbles, for sediments.

Addendum.

Concretions.

By concretions we mean hard, stony bodies, made up either of normal or abnormal constituents of urine. These vary greatly in size, from such as can hardly be discovered through the microscope, to some which are as large, or larger, than the fist.

Every concretion, whatever its size, will show a deposit of molecules in layers, and must, of necessity, be more or less rounded. The cystin calculus, which, upon section, shows a crystalline structure, is the only exception to this rule. In order to convince ourselves

upon this point, either a lense or a microscope must be called into requisition. Concretions of uric acid are frequently found which, with the naked eye, might easily be mistaken for a conglomerate of uric acid crystals (rosette). Concretions of calcium carbonate are also found, whose arrangement in layers is only visible when a power of 100 or 200 diameters is used.

Small concretions usually come from the kidney. Larger ones, from the bladder.

Calculi are made up either of one constituent solely, or of several, arranged in layers. Thus, uric acid calculi usually consist, throughout, of uric acid or its salts; cystin calculi of cystin; while the oxalates frequently have a nucleus of uric acid and an outer layer of phosphates; and the phosphates, a nucleus of uric acid.

It is immaterial whether one or more substances are used for the formation of the calculus; we are always in a position to distinguish the nucleus.

In order to examine the structure of the calculus, it is necessary to cut it by means of a fine watchmaker's saw. The innermost layer is the nucleus, which varies in size from a millet seed to that of a pea, or over, and shows to greatest advantage when surrounded by a layer of structures different from its own.

The nucleus is the most important part of the calculus, as it alone gives definite knowledge regarding the genesis of the stone. If we find an uric acid nucleus in a phosphatic calculus, we will know that calculus formation was caused by uric acid; if we find

a foreign body, as a piece of catheter or bougie, we may know that this was the primary cause.

From a surgical stand-point, calculi are divided according to their principal constituent; thus, calculi of urates, oxalates, phosphates and cystin. This division is of great practical importance, for, if a surgeon states that a calculus is phosphatic, he, at the same time, implies that it is soft; if oxalate or urate, that it is hard.

But as calculi exist that are made up of three or more calculus-forming substances, it might embarrass the surgeon to say to which group they belong; it is better, therefore, to divide all calculi into two groups, characterized by their nuclei.

One group contains all those calculi whose nuclei are formed by the sediments of acid urine; the second, those whose nuclei are either foreign bodies, coagula of blood, or constituents of alkaline urine.

This division agrees with what is known as primary and secondary calculus-formation; primary being the first, and secondary, the second group, to which latter is added the incrustation of a calculus from the kidney, in the bladder. Primary calculus-formation takes place only in the kidney; secondary, almost always, in the bladder.

A separate class is formed by the so-called metamorphous calculi, which consist of earthy phosphates, and form a homogeneous, porous mass. These are always the result of a purulent process, of years continuance, in which the sediment of acid urine has been dissolved by alkaline pus, and substituted by the earthy phosphates.

Primary formation is principally begun by uric acid, the majority of calculi of the bladder having a nucleus of it.

In 545 calculi from the bladder, Ultzmann has found the nucleus to have the following composition:

Uric Acid,................	441	or	80.9%
Calcium Oxalate,..........	31	or	5.6%
Earthy Phosphates,........	47	or	8.6%
Cystin,...................	8	or	1.4%
Foreign bodies,...........	18	or	3.3%

Analysis.

Every calculus must be divided into two equal parts with a saw. The dust from the sawing must be mixed, collected, and examined by the key which follows. In this way all the principal constituents are discovered, but not their arrangements.

In order to determine this, one-half is polished upon a glass plate until the various layers can be easily distinguished. From each layer sufficient quantity is scraped off with a pen-knife, and this is examined separately. An illustration will make this clearer.

It has been determined that the $\frac{1}{2}$ of a calculus is made up of $\frac{2}{3}$ inorganic (non-combustible), and $\frac{1}{3}$ organic substances. Furthermore, the following substances have been detected: Uric acid, oxalic acid, phosphoric acid, calcium, magnesium and ammonium. On polishing, we now find three layers. The nucleus, by the proper test, is found to consist of uric acid; the dark-brown middle layer, of calcium oxalate, and the

white outer layer, of calcium carbonate and phosphates, and magnesium.

The method for analysis is as follows:

A few millegrammes of the powder are heated to redness on platinum. In this test be careful to observe whether or not a deposit is left after burning; whether or not a visible flame is produced; whether the substance crackles (calcium oxalate), and whether it gives off a characteristic odor.

I. When *no* deposit is left after burning, the following substances may be present: Uric acid, sodium and ammonium urates, xanthin, proteïn and cystin.

1. *Proteïn* gives off, when burnt, a yellow, luminous flame, and an odor like burnt feathers or hair.

2. *Cystin* burns with a faint, bluish-white flame, and produces a penetrating odor, as of burning fat and sulphur. The powder is soluble in diluted ammonia, and upon evaporation shows the characteristic crystal.

3. *Xanthin*, with the murexid test, produces a pomgranate-yellow color, and burns without visible flame.

4. *Uric Acid*, sodium urate and ammonium urate, give the characteristic murexid reaction.

(*a*) *Sodium Urate* can be distinguished from the ammonium urate, and from uric acid, as follows: At the spot on the platinum where the urate is burnt, a slight haziness remains; a piece of red litmus paper, moistened, and put upon this spot, will turn blue immediately, wherever it touches the haziness. This reaction is probably due to the presence of sodium

carbonate or hydrate, formed by the decomposition of sodium urate.

(*b*) *Ammonium Urate* can be distinguished by the detection of ammonium. Some of the powder is moistened by potassium hydrate, and a piece of red litmus paper, which the escaping ammonium will turn blue, is suspended over it.

(*c*) *Free Uric Acid* gives negative results with both of these tests.

II. When the powder *burns incompletely*, or not at all, it consists chiefly of calcium and magnesium salts. The following are found in the form of calculi: Calcium oxalate, calcium carbonate, calcium phosphate, and triple phosphates.

1. *Calcium Oxalate* does not effervesce when hydrochloric acid is added. When heated we notice a peculiar glowing, and a crackling sound. By heating, the oxalate is converted into a carbonate, and the addition of hydrochloric acid will cause a decided effervescence.

2. *Calcium Carbonate* will effervesce without being heated, upon the addition of hydrochloric acid.

3. *Calcium Phosphate* and the *Triple Phosphate* neither effervesce before or after heating, but hydrochloric acid will entirely dissolve the powder after heating. If ammonium hydrate is added until the solution becomes alkaline, a flaky precipitate of amorphous basic calcium phosphate, and crystalline triple phosphate, will be found. Under the microscope, the latter is shown to consist of crystals in the form of stars and crosses.

CHAPTER IV.

Reagents and Apparatus for the Approximate Examination of the Constituents of Urine.

It is best to have wide-necked bottles, with ground stoppers, holding 250 c. c. of fluid. We give the reagents in the form of prescriptions:

(*a*) Acids.

1. Acid. hydrochloric. C. P., 200.00.
2. Acid. sulphuric. C. P., 200.00.
3. Acid. nitric. C. P., 200.00.
4. Acid. acetic. C. P., 200.00.

(*b*) Bases and Salts.

5. Potass. fus. pur., 100.00.
   Aquæ destillat., 200.00.
6. Ammon. pur. liquid, 100.00.
7. Barii chlorid. cryst., 30.00.
   Aquæ destillat., 200.00.
   Acid. hydrochloric, 10.00.
8. Plumbi acetat. cryst., 30.00.
   Aquæ dest., 200.00.
9. Cupri sulphat., 30.00.
   Aquæ destillat., 200.00.
10. Magnesiæ sulphat.
    Ammonii chlorid. pur. āā, 30.00.
    Aquæ destill., 200.00.
    Ammon. pur. liquid, 50.00.
11. Argenti nitrat., 5.00.
    Aquæ destill., 40.00.
12. Red and blue litmus paper, cut in strips.

Besides these necessary reagents, it is also well to keep the following, for special cases: Distilled water, ferric chloride, zinc chloride, basic lead acetate, mercuric nitrate, bismuth sub-nitrate, fuming nitric acid, potassium nitrite, starch, chloroform, ether, alcohol, iodine dissolved in potassium iodide, glacial acetic acid, sodium chloride, etc.

Apparatus.

1. Six test-tubes and stand.
2. Ten wine glasses (such as are used for sherry wine).
3. Cylinder glasses, with a capacity of 100, 200, and 300 c. c.
4. A graduated cylinder.
5. A flask with capacity of 100 c. c., with cork perforated by a glass tube.
6. An urinometer (areometer).
7. A spirit lamp.
8. Two small porcelain dishes.
9. A brass stand, with two rings.
10. Filter paper.
11. Four funnels.
12. Glass rods.
13. A microscope.
14. A glass vessel, with capacity of 3,000–4,000 c. c.

Watch glasses, beakers and pipettes. For quantitative purposes, apparatus for volumetric analysis are also needed.

CHAPTER V.

Quantitative Detection of Urinary Constituents.

The one condition necessary for all quantitative estimations, is the exact collection of all the urine passed within a given time. It is usually collected

during twenty-four hours, and in order to prevent its mixture with feces, it is passed before defacation.

It is inadvisable to multiply the quantity for one hour, in order to estimate that of any number of hours, as the quantity of urine varies with different parts of the day.

Urine is collected in graduated cylinders. In order to find the average of excretion of any patient, the urine for several successive twenty-four hours should be collected and averaged.

I. Estimation of Acidity.

To estimate the degree of acidity, a solution of sodium hydrate must be added, until neutral reaction sets in; then find out how much of any acid (best, oxalic acid) is required to neutralize the quantity of alkali used.

(*b*) *Test Solution.*

An $\frac{1}{10}$ solution of sodium hydrate, which contains 0.0031 grammes NaO in 1 c. c., is necessary to neutralize 6.3 mille-grammes of crystallized oxalic acid.

(*b*) *The Test.*

Measure off 100 c. c. of urine in a beaker, then add, with a burette, the above solution until the reaction to litmus is negative. The number of c. c. used is multiplied by 0.0063. This product shows the acidity of 100 c. c. of urine reduced to oxalic acid.

II. Total Solids.

Ten c. c. are evaporated to dryness, over a water bath, in a porcelain dish which has been weighed, this kept at 100° C. in the air-bath for an hour, then allowed to cool under a dessicator, and weighed. Again dried and dessicated and weighed, and this operation repeated until no diminution in weight is observed. The difference between this weight and that of the dish represents the weight of the solids in 10 c. c. of urine. Unfortunately, the result is not accurate on account of the reaction of the acid sodium phosphate upon urea, producing, at 100° C., carbonic acid gas and ammonia, which are lost.

Usually the approximate means are sufficiently exact for the practicing physician. If not, the method of Neubauer ought to be used. (See Neubauer and Vogel, Analysis of Urine.

III. Urea.

1.—The Method of Liebig.

(a) *Reagents.*

1. *Barium Solution.*—One vol. of saturated (cold) solution of barium nitrate is mixed with 2 vol., cold, saturated solution of barium hydrate.

2. *Titrate for Urea, i. e.*, solution of pure mercuric nitrate, of the concentration that 71.48 gr. of pure mercury, or 77.2 gr. of mercuric nitrate; dried, at 100° C., are contained in 1 litre. (For preparation see Neubauer and Vogel.)

Solution of Sodium Carbonate.—For Raudenberg's modification, acid sodium carbonate must be used. This is stirred up in water, after having been rubbed up finely and washed by small quantities of water until turmeric is no longer turned brown.

(*b*) *The Test.*

With a pipette, 40 c. c. of urine are taken, and 20 c. c. of the barium solution added. A precipitate of phosphates and sulphates will result. Allow this to stand, and then filter into a dry vessel through dry paper. The filtrate is composed of one-third barium solution, and two-thirds urine, from which the phosphates and sulphates have been removed. Of this mixture, 15 c. c. are poured into a dry vessel (only two-thirds, or 10 c. c., are urine), and the solution of mercuric nitrate is allowed to flow into it from a burette. Having used as many c. c. of the solution as are indicated by the last two figures of the specific gravity of the urine examined (thus 13 c. c. if sp. gr. is 1.015), it is necessary to see whether or not the limit has been reached.

Put a drop of the mixture into a porcelain dish, and add to it a drop of sodium carbonate. If a rusty zone is produced where the fluids meet, continue to add the test fluid; if this zone is pale, do not continue, for the work has been completed.

The chemical process is as follows: On the addition of mercuric nitrate $Hg(NO_3)_2$ it first seeks the chlorine contained in the common salt in urine, forming $HgCl_2$ (corrosive sublimate).

$$Hg\begin{cases} NO_3 \\ NO_3 \end{cases} + \begin{matrix} NaCl \\ NaCl \end{matrix} = HgCl_2 + 2NaNO_3$$

The $NaNO_3$ remains in solution, but the $HgCl_2$ is precipitated, the solution being alkaline. After all the NaCl has

been converted into $HgCl_2$, the mercuric nitrate forms a combination with the urea, by which NO_3 is liberated, which upon the addition of sodium carbonate, takes the place of the carbonic acid, which escapes in fine bubbles. $NaNO_3$ does not change the color of the precipitate in the porcelain dish. But if the limit has been reached, where all the mercuric nitrate is bound to the urea, and a drop of the mixture with urine is added to sodium carbonate, mercuric oxide will be precipitated, at the same time $NaNO_3$ being formed, and CO_2 escaping:

$$Hg(NO_3)_2 + Na_2CO_3 = HgO + CO_2 + 2NaNO_3.$$

HgO is precipitated as a brownish powder, which, as we now comprehend, forms the limit test for the reaction.

Having completed titration, the burette is allowed to stand *for a few minutes*, and we then read off how many c. c. have been used.

The fluid is so arranged that 1 c. c. satisfies 10 millegrammes of urea, exactly. If we had used 20 c. c. there would be present 200 mgr. of urea in the mixture (15 c. c.), which was made up of 10 c. c. urine and 5 c. c. barium fluid. From this can be computed, without difficulty, how much urea is passed in twenty-four hours.

1. As the test fluid is fixed for a 2% solution of urea, we can only obtain accurate results when for 15 c. c. of a 2% solution of urea, there is used exactly 30 c. c. of the mercury solution, of which 1 c. c. represents 10 mgr. of urea, exactly.

Every c. c. of the solution requires for the satisfaction of 10 mgr. of urea, 72 mgr. HgO. In order, however, to produce the terminal reaction, there must be an excess of HgO. According to Liebig, this amounts to 5.2 mgr. for 1 c. c. of the solution, for 30 c. c. $30 \times 5.2 = 156$ mgr. If, now, to 15 c. c. of a 2% solution of urea, 30 c. c. of the solution are added, the mixture amounts to 45 c. c., in which there are 156 mgr. of

HgO in excess, *i. e.*, 3.56 mgr. for each c. c. In order to effect a positive terminal reaction, then, it is necessary to have in each c. c. of mixture 3.46 mgr. of HgO in excess.

If the 15 c. c. of urea solution have 3.5% urea, 52.5 c. c. of the mercury solution would be required. The quantity of the mixture then would be 15 c. c. + 52.5 c. c. = 67.5 c. c.; in the 52.5 c. c. of solution is present $52.5 \times 5.2 = 273$ mgr. of HgO in excess, in every c. c. of the mixture; therefore, 4.04 mgr. But the termination of the reaction takes place with 3.46 mgr., we therefore have 0.58 mgr. too much. In this way the terminal reaction sets in too early.

If the solution only contains 1% of urea, the error would be in the other direction.

In order to eliminate both errors, we proceed as follows:

(*a*) If more than 30 c. c. of the test solution is required, add half as much water as the number of c. c. of test solution is more than 30 before testing with the sodium. Thus, as 52.5 c. c. have been used, we add $\frac{22.5}{2}$=11 c. c. of water to the mixture before testing with soda.

(*b*) If less than 30 c. c. were sufficient, then we deduct for every 5 c. c. less than 30 c. c., 0.1 c. c. from the whole quantity used. Thus, if we use 20 c. c. (10 c. c. less) we compute with $20 - 0.2 = 19.8$ c. c.

2. If the urine contains 1—1.5%, $NaCl$, the formation of corrosive sublimate will necessitate an increased amount of the test solution, which, without being corrected, would give too great an amount of urea (15 to 25 mgr.). In order to correct this error, subtract 2 c. c. from the figures read off from the burette.

If we wish to get absolutely correct results, we must either first titrate the $NaCl$ with a nitrate of silver solution, or use Raudenberg's method. According to this, two tests are made, for each of which 15 c. c. of mixture are prepared. The one is acidulated with nitric acid, and the mercuric nitrate solution is added until the cloudiness remains permanent. With the second test we proceed according to Liebig, with the

addition of keeping the mixture neutral by means of freshly precipitated calcium carbonate. For the terminal reaction, the solution 3 (sodium carbonate) is employed. We now subtract the c. c. used in the first test from the number used in the second, and from this we calculate the quantity of urea.

3. If albumin is present, 20 c. c. are placed into a vessel that can be closed, a few drops of acetic acid added, and then boil until the albumin separates in coarse flakes; now close the vessel and allow to cool. Finally, filter, and proceed as before.

II. Method of Bunsen (Bunge).

Only to be used when neither sugar nor albumin are present. Fifty c. c. of urine are precipitated with an ammoniacal solution of barium chloride, filtered, and 15 c. c. of this put into a tube with thick walls. Upon the bottom of the tube are three grammes of crystallized barium chloride. Seal the tube and heat to 200° C. for six hours in an oil-bath. After cooling, break off the point of the tube, pour the contents upon a filter, wash out the barium carbonate that has collected, and dissolve it in a sufficient quantity of hydrochloric acid. Care must be taken to wash off and dissolve any barium carbonate that may be found adhering to the walls of the tube. All of the solution is filtered and precipitated with sulphuric acid, the precipitate of barium sulphate collected, washed, heated and weighed.

Two hundred and thirty-three grammes of barium sulphate, representing 60 grammes of urea, we can easily compute the quantity of urea present.

III. Method of Knop-Hüfner.

(*a*) *Solutions.*

1. *Hypobromite of Sodium.*—One hundred grammes of sodium hydrate are dissolved in 250 c. c. of water, and mixed

with 25 c. c. of bromine. This must always be prepared fresh.

2. *A saturate solution of common salt.*

(*b*) *Test.*

Dilute 10 c. c. of urine with 40 c. c. of water, fill the lower cup, and the cork, of Hüfner's apparatus with urine, fill the upper part with the hypobromite solution, and the vessel above with the salt solution, and into it put the eudiometer. After five minutes the development of gas ceases. After one hour the eudiometer is taken off, and the quantity of urea is calculated, according to the method of Dumas, 1 gramme of urea producing 370 c. c. of nitrogen (at 0°C and 760 m.).

IV. Estimation of Uric Acid.

To 300 c. c. of urine are added 10 c. c. of hydrochloric acid; this is well stirred, and allowed to stand in a cool place for forty-eight hours. Albumin, if present, must be removed; if the urine contains sugar, it must be treated with mercuric acetate; the precipitate, being washed on a filter, is mixed with a little water; hydrogen di-sulphide is allowed to act on it, when it is again filtered. The mercuric sulphide is washed with warm water, and this water is treated like the urine. The crystals of uric acid are collected on a filter paper which has been washed with water and acetic acid, dried between two watch-glasses at 100° C., and then weighed. As uric acid crystals are very heavy, they can be collected by decanting the fluid; the crystals which adhere to the walls of the vessel can be removed with a feather, when they will

fall to the bottom. Only when the crystals are very small is it necessary to filter.

Uric acid is washed with distilled water until the filtrate no longer produces a reaction with silver nitrate. It is better to use not more than 30 c. c., otherwise some of the uric acid is dissolved. If more than 30 c. c. have been used, 0.045 mgr. for each c. c. of water used must be added to the whole amount of uric acid found.

The uric acid is now dried at 100° C., between watch-glasses, in the air-bath, dried in the dessicator, and weighed.

The difference between the two weighings represents the weight of uric acid contained in 300 c. c. of urine.

Schwanert recommends adding for every 100 c. c. of urine employed, 0.0048 grammes, claiming that the result is more correct.

V. Estimation of Creatinin.

(*a*) *Reagents.*

1. *Zinc Chloride Solution.*—Pure zinc oxide is dissolved in pure hydrochloric acid; this solution is evaporated in the water-bath to the consistency of syrup (until no free acid can be detected), dissolved in strong alcohol until specific gravity of 1,200 is reached.
2. *Milk of Lime.*—To be shaken before using.
3. *Dilute Solution of Calcium Chloride.*

(*b*) *Test.*

Two hundred c. c. are rendered alkaline with the milk of lime and the calcium solution added as long as a precipitate

is formed. After two hours, filter, wash and concentrate everything having come through the paper, in the water-bath, to the consistency of a thick syrup. Add, while warm, 50 c. c. of alcohol (95)%, pour into a beaker and allow to stand for eight hours. Again filter and wash, and evaporate to 60 c. c. After cooling, add ½ c. c. of the zinc chloride solution, stir with a glass rod and allow to stand forty-eight hours. A compound with zinc chloride is formed, which is treated like the crystals of uric acid. In 100 parts of this compound are found 62.44 parts of creatinin.

VI. Estimation of Total Nitrogen.

The principal amount of nitrogen in urine is contained in urea, and as Liebig's method includes other nitrogenous substances, this usually suffices.

The direct method is usually performed by burning with soda-lime.

(*a*) *Reagents.*

1. *Fresh Soda by Lime.*
2. *Normal Sulphuric Acid*, containing 40 grammes of sulphuric acid anhydride in 1 litre of water, every c. c. corresponding to 0.014 grammes of nitrogen. (See Neubauer and Vogel.)
3. *Solution of Caustic Soda*, equivalent to the sulphuric acid, *i. e.*, 10 c. c. of the one must neutralize 10 c. c. of the other.
4. *Litmus Tincture.*

(*b*) *Test.*

Pour 20 c. c. of sulphuric acid into a beaker and then suck the greater part into the nitrogen apparatus of Will-Varrentrapp. Into a flask holding 100 c. c., soda lime to the depth of 2 c. c., and 5 c. c. of urine are put, the flask closed with a cork having two openings, and the whole placed into a sand-

bath. Through the one opening of the cork the connecting tube with the nitrogen apparatus passes, through the other passes a fine tube, drawn out at one end and closed. Heat the sand-bath as long as bubbles of gas pass through the apparatus. When this has ceased, break off the end of the fine tube and draw out all the ammonia from the flask. Now the contents of the apparatus are poured into the beaker before mentioned; put a few drops of the litmus tincture into the fluid, and add the caustic sodium solution until the red color is changed to blue.

If, by decomposition, no ammonia had been formed, we would have to have added 20 c. c. of soda to neutralize the 20 c. c. of normal sulphuric acid. If 14 c. c. only are necessary, in proves that 6 c. c. of sulphuric acid have been satisfied by the ammonia formed, 1 c. c. corresponding exactly to 0.014 grammes of nitrogen, the quantity of N. present will equal $6 \times 0.014 = 0.084$ grammes N. in 5. c. c. of urine. From which the quantity passed in twenty-four hours can easily be found.

VII. Estimation of Albumin.

Filter the urine and take 100 c. c. (where little albumin is present), 50 c. c. (where more is present, dilute with 50 c. c. of water), or 20 c. c. (where great quantities are present dilute with 80 c. c. of water), which is to be heated for half an hour in the water-bath. If the albumin does not come down in coarse flakes, add 1–2 drops of acetic acid, and continue to heat. Allow the fluid to pass through a weighed filter, and wash with distilled water until the wash-water ceases to show the NaCl reaction with $AgNo_3$. The filter is then dried between watch-glasses at 100° C., and weighed.

VIII. Estimation of Sugar.

FEHLING'S METHOD.

(*a*) *Solution.*

Fehling's Solution.—In 1,000 c. c. are contained 30,639 grammes cupric sulphate, 173 grammes pure, crystallized tartrate of sodium and potassium, and 500 grammes of solution of caustic soda (sp. gr. 1.12). Ten c. c. of this solution are reduced by 0.05 gr. of sugar.

(*b*) *Test.*

The estimation of sugar depends upon the property of grape sugar of reducing cupric sulphate in the presence of an alkali. For this purpose urine is filtered, and, if the quantity of sugar present is not too small, it is diluted with water. Usually 10 c. c. of urine are diluted with 190 c. c. of water. A burette is filled with this mixture. A flask, or porcelain dish, is placed upon a wire net, and into it is put 10 c. c. of Fehling's solution, diluted with 40 c. c. of water. Now heat, and as soon as it boils, add the urine, drop by drop. Gradually the fluid becomes yellow, then red; finally, all the blue disappears, and the red cuprous oxide precipitates very quickly. If allowed to stand a little while the solution will be found entirely colorless, unless too much urine has been added, in which case it will be slightly yellow. The entire discoloration, then, is the terminal reaction.

As this can not always be readily determined with the naked eye, it is advisable to filter a few drops into

a test-tube, testing one part of the fluid, after acidulating it with acetic acid, with potassium ferro-cyanide for copper, and the other with Fehling's solution for sugar. If neither are present, then the reaction has been completed.

In the estimation for sugar it is essential to compute the amount of urine employed.

Supposing that we have used 25 c. c. of the urine mixture to reduce 10 c. c. of Fehling's solution. The mixture was so prepared that 200 c. c. contained only 10 c. c. of urine. In order to ascertain how much urine there is in 25 c. c. of the mixture, we institute the following proportions:

$$200 : 10 :: 25 : x. \quad x = 1.25 \text{ c. c.}$$

Therefore, 1.25 c. c. of urine was able to reduce 10 c. c. of Fehling's solution, completely. But the solution is so arranged that 10 c. c. will reduce 0.05 gr. of sugar; 10 c. c. of the solution being reduced by 1.25 c. c. of urine, the latter must contain 0.05 gr. of sugar. From these data we can easily compute how much sugar is passed in twenty-four hours.

If albumin is present it must be removed by the method already described.

Note.—When Fehling's solution has been kept for some time, it becomes self-reducing. It is therefore necessary to boil the solution in a test-tube before using, and if reduction does not take place, it may be used for the test. The solution will retain its delicate properties for years, if it is placed in hermetically sealed glass bottles (containing about 15 c. c.) and kept in a cool place.

There are various methods of preparing this solution extemporaneously. While they may be very serviceable to the chemist, who always has his chemicals ready for use, to the physician the above mentioned method of preservation will, I think, recommend itself. The tablets, consisting of the

compressed salts which go to make up Fehling's solution, and held together by some inert substance, I have never used, always finding my small bottle in good condition. (Tr.)

2.—KNAPP'S METHOD.

(a) *Solution.*

Ten grammes of pure mercuric cyanide are dissolved in a little water. To this is added 100 c. c. of a solution of sodium hydrate (sp. gr. 1.145), and the whole diluted to 1,000 c. c.; 40 c. c. of this solution reduce 100 milligrammes of sugar.

(b) *Test.*

Heat 40 c. c. of the solution in a beaker, and add diluted urine, as in Fehling's test, until the originally clouded mixture becomes clear and yellowish. From time to time, a drop should be taken out and tested with ammonium sulphide. As soon as the spot no longer shows a brown circumference, the test is complete. Fehling's method and this one give results which do not exactly correspond.

The fermentation method is much more laborious, and not as exact, as Fehling's. Very accurate results are obtained with the saccharimeter of Soleil-Ventzke, or the polaris trobometer of Wild. (See Neubauer and Vogel.)

IX. Estimation of Chlorine.

1—AFTER MOHR.

(a) *Reagents.*

1. Saturated solution of potassium chromate.
2. Titrated solution of silver nitrate, containing 29,075 gr. of $AgNO_3$ (18,469 gr. Ag) in a litre, so that 1 c. c. represents 10 mgr. of NaCl (=6,065 mgr. Cl).
3. Calcium carbonate.

(*b*) *Test.*

Ten c. c. of urine are measured into a platinum crucible; add 2 grammes of pure nitre, evaporate to dryness over a water-bath, heat over a Bunsen's burner until the melted mass no longer contains any carbon. Dissolve in a little water and carefully rinse the crucible. Solution and rinsings are carefully collected in a beaker, nitric acid, free from chlorine, is then added until a weak acid solution is produced, which is then neutralized, carefully, with freshly precipitated calcium carbonate. Without regard to the precipitate, three drops of chromate solution are added, and then the silver solution is allowed to flow into the mixture. As soon as the yellowish fluid becomes reddish, it is a sign that all the common salt has been converted into chloride, and that the formation of silver chromate has begun. At this moment the work is completed.

If for 10 c. c. of urine we had used 9.6 c. c. of the titrated fluid, we would have 96 mgr. of NaCl present, as 1 c. c. of the fluid indicates 10 mgr. NaCl.

From this we can readily determine how much NaCl present in twenty-four hours.

If the patient has been receiving iodine or bromine preparations, it becomes necessary to remove these from the urine. In order to carry this out, add to the solution, as it comes from the crucible, sulphuric acid, then a few drops of potassium nitrite, then shake with bi-sulphide of carbon as long as this takes up I. or Br., then neutralize with natrium carbonate, and proceed as above.

X. Estimation of Phosphoric Acid.

(a) *Reagents.*

1. *Solution of Sodium Acetate.*—One hundred grammes of the salt dissolved in 900 c. c. distilled water and 100 c. c. of concentrated acetic acid added.
2. *Solution of Uranium Nitrate*, 1,000 c. c. containing 20.3 gr. pure uranic oxide; 1 c. c. represents 5 mgr. of phosphoric acid.
3. *A Solution of Potassium Ferro-Cyanide.*

(b) *Test.*

Fifty c. c. of urine are measured into a beaker, mixed with 5 c. c. of the solution of sodium acetate, and heated in a water-bath. Then add the uranium solution as long as a precipitate continues to form. If this point can not be determined accurately, place a few drops upon a porcelain dish, and, if upon addition of the potassium ferro-cyanide, a brownish-red boundary line is produced, cease adding the uranium solution and again heat in a water-bath. See if a precipitate will now form. Usually this is not the case; then a few drops of the uranium solution are added so that the ferro-cyanide test succeeds with the boiling mixture. The border reaction then sets in, when all the phosphoric acid has been precipitated by the uranium, in that the next drop, finding no acid, is precipitated brown by the ferro-cyanide of potassium.

If we have used 13 c. c. of the solution, for instance, we could establish the following proportion (1 c. c. = 5 mgr. of phosphoric acid):

$$1 : 5 :: 13 : x; \quad x = 65 \text{ mgr.}$$

From which, the quantity of urine in twenty-four hours being known, the amount in twenty-four hours can be easily computed.

If we wish to determine the phosphoric acid that is bound to the earths, 200 c. c. of urine are precipitated with ammonia. The precipitate is collected; after twelve hours, upon a filter, washed with aqua ammoniæ (1 part in 3 of water), the filter perforated, and the precipitate washed into a beaker. The precipitate is then dissolved with a small quantity of acetic acid, 5 c. c. of the solution of sodium acetate added, diluted to 50 c. c. and examined as above.

The difference between the total phosphoric acid and the phosphoric acid in combination with the earths, will give the phosphoric acid united with the alkalies.

XI. Estimation of Sulphuric Acid.

One hundred c. c. of urine, heated and precipitated with barium chloride, and the barium sulphate which is formed, collected on a filter of known weight, washed, burnt in a crucible whose weight is also known, moistened with a few drops of sulphuric acid, and again heated. Then the whole is weighed, the difference between total weight and the weight of crucible + filter, representing the weight of barium sulphate. As 34.33 parts, by weight, in 100 parts of barium sulphate, represent sulphuric acid, the latter can be easily determined.

For exact quantitative tests, see Neubauer and Vogel, Hoppe-Seyler, etc.

CHAPTER VI.

Key to the Approximate Analysis of Urine.

After having allowed the urine to stand for several hours, we first determine its physical properties:

1. The quantity in twenty-four hours.
2. Color and transparency.
3. Odor.
4. Reaction to litmus.
5. Specific gravity.
6. Quantity of sediment.

If a sediment has been formed, it is examined after the urine is poured off. If very cloudy, the urine must be filtered, and if the filtrate is still cloudy, heating slightly will clear it. The sediment is kept for further examination.

Chemical Examination.

About 15 c. c. of clear urine are taken, and 5 c. c. of pure nitric acid are allowed to flow under it. We find, by this test:

1. Albumin.
2. The urates.
3. Biliary coloring matters.
4. Indican.

When much iodine is present, the ring of coloring matter between the nitric acid and the urine is colored

yellowish-brown, and the odor of iodine is distinctly present.

Very minute quantities of these substances are only separated after some time; it is, therefore, of importance to put the vessel aside, and examine the result after a little time has elapsed. The next is the

(*b*) Test by Boiling.

Fill a test-tube one-third full with clear urine, and boil over a lamp. If turbidity is produced, there is present either albumin or the earthy phosphates. Add 1–2 drops of acetic acid; the phosphates are dissolved —not so the albumin. Now add liquor potassæ, one-half the quantity that we added of urine; albumin dissolves, but, at the same time, the earthy phosphates are brought down in the form of fine flakes. Now boil again. If the mixture becomes brown, sugar is present; if this does not occur, put the test-tube on a stand, and, after having allowed the precipitate to settle, determine its quantity and color.

In normal urine this always is white; if colored, then there may be present various coloring matters. If it appears blood-red or dichroic, then blood-coloring matter is present. In confirmation, albumin must be present, and hæmin crystals must be detected by the proper methods. Nearly always, blood corpuscles will be detected.

If the precipitate is pink, and the urine does not contain albumin, then vegetable coloring matter is present (especially after taking senna or rhubarb). In

order to verify this, the urine must, upon addition of ammonia, become reddish, which will again disappear when acids are added.

If the precipitate is grayish, then uroërythrin, the coloring matter of fever urine, is present. This is verified by the presence of a brick-dust sediment, or the production of a reddish or flesh-colored precipitate upon the addition of a solution of lead acetate.

A brown color of the precipitate indicates biliary coloring matter. If the same is not decomposed, Heller's test will give a beautiful play of colors. If this fails, it is decomposed; the sulphuric acid test must then be increased in proportion as the specific gravity is low, and a mixture of urine with potassium hydrate will appear darker.

(*c*) Test for Normal Coloring Matter of Urine.

1. Test with concentrated sulphuric acid (Heller's Uropaeïn).
2. Test for indican with concentrated hydrochloric acid and calcium chloride solution.

(*d*) Test for the Normal Inorganic Salts.

1. For the chlorides. The vessel in which the test (*a*) has been performed can be used; the two layers are stirred with a glass rod, and then one or two drops of the silver nitrate solution are added.
2. For the *alkali* phosphates with the magnesia fluid, and
3. For the *sulphates*, with barium chloride.

(*e*) Test for Abnormal Substances.

If necessary, test for *ammonium carbonate*, *sodium carbonate*, *hydrogen di-sulphide*, *leucin* and *tyrosin*. These can be determined by the preceding tests.

(*f*) Examination of the Sediment.

First determine color and consistency of sediment, (whether crystalline, a powder, flaky, etc.); then its composition. This can either be done chemically, or better, microchemically and microscopically. Finally, we determine the organized admixtures (epithelium, casts, spermatozoa, etc.).

Having examined an urine according to this method, it is of importance, especially for the beginner, that all the results are noted in a brief and schematic way, so that an oversight can be had, and the result easily deduced.

The following method can be used to great advantage:

Physical Properties.	
Normal Substances.	
H_2SO_4 Test.	Cl
Ind. "	Eph.
$\overset{+}{U}.$	Aph.
$\overline{U}.$	Sph.
Abnormal Substances in Solution.	
Sediment.	
Result.	

Divide a sheet of paper into four parts; the upper for the examination of the physical properties, the second for the quantity of normal constituents present. The abbreviations employed are as follows:

H_2SO_4 test	= Sulphuric acid test for coloring matter.
Ind.	= Indican.
$\overset{+}{\text{U}}$.	= Urea.
$\overset{—}{\text{U}}$.	= Uric acid.
Cl.	= Chlorides.
Eph.	= Earthy phosphates.
Aph.	= Alkaline phosphates.
Sph.	= Sulphates.

To express whether a substance is present in normal, greater or smaller quantity, the following signs are employed: For an increase, +; for diminution, the sign —; for normal, the letter "n". Great increase or diminution are represented by "gr.+" and "gr.—;" also, a moderate increase or diminution by "m +" and "m —."

The third division is for the normal substances found in solution.

The last for the description of the sediment and the result, the diagnosis. A sheet of paper, filled out, looks like the following:

PHYSICAL PROPERTIES.

Quantity = 4,000 c. c.
Pale yellow, somewhat cloudy, acid.
Sp. gr. = 1,040; slight sediment.

H_2SO_4 test -	gr.—	Cl. - - -	m.—
Ind. - - - -	m.+	Eph. - -	gr.—
$\overset{+}{U}$. $\overline{U}$. - - -	m.—	Aph. Sph. -	m.—

ABNORMAL SUBSTANCES IN SOLUTION.

Sugar in large quantities.

SEDIMENT.

Consists of mucus in normal quantity.
Microscopically, a few yeast fungi are detected.

RESULT:— Diabetes Mellitus.

Using a blank like the above will facilitate, not only the analysis but also the diagnosis. Coming back to the above, we deduce as follows:

1. From the quantity in twenty-four hours; *Polyuria.*

2. From the specific gravity, and the amount of solids found by computation from it; *Diabetes.*

3. From the pale color and absence of the urates; *the absence of fever.*

4. Finally, from the presence of sugar; *Diabetes mellitus.*

CHAPTER VII.

General Diagnosis.

At the time when the examination of urine consisted solely in an observation of its physical properties, undertaken with preconceived notions of what would be found, and when the so-called "urine signs" were forced into a ready-made system which had naught but chimeras for its foundation, it was no aid to the discovery of pathological processes, and served rather, as a cover for ignorance and quackery.

It is only since organic chemistry and microscopy have progressed; since the connection between the composition of urine and the changes in the economy, on the one hand, and the structure of the urinary apparatus, on the other, have been thoroughly recognized, that the analysis of urine can be termed a scientific procedure. Its value in diagnosis is now undoubted; in some cases, it alone gives insight into the stage, the nature, and the intensity of the disease. It would, indeed, be an error to suppose that all diseases could be diagnosticated by means of the urine, but it would be equally unjustifiable to neglect its examination entirely.

Before proceeding to the diagnosis of the diseases of

the urinary organs, we will first mention those rules which are important to urinalysis in general, taking them up in the order in which they will be of most value to the practicing physician.

1. Measure the quantity of urine passed in twenty-four hours, and determine whether normal, increased or diminished. The *normal quantity* is about 1,500 c. c.; if the quantity is very much above this, we have *polyuria;* if very much below, *oliguria*, and if no urine whatsoever is passed, *anuria.*

Polyuria may be *physiological* or *pathological.* In the former instance it is *urina potus* or *urina spastica*, and in the latter, *hydruria* or *diabetes.* In order to make this differential diagnosis we compute the amount of solids in twenty-four hours, by *Trapp's* or *Haeser's* coëfficient. If this amount is nearly normal (70 gr.), then we have an *urina potus*, *i. e.*, an urine with normal solids that has been diluted. If the solids are diminished, then it is *hydruria*, as observed in many cachexias. If the solids are very much increased, then we have *diabetes;* sugar being detected, in appreciable quantity, in the latter instance, it is *diabetes mellitus*, no sugar being present, *diabetes insipidus* (when the nitrogenous substances are increased, *azoturia*).

Oliguria can be readily diagnosticated, and occurs principally in febrile diseases. The urine usually is dark and very much concentrated. In the last stages of disease of the kidney, when uræmia sets in, the quantity of urine is always diminished. A mild form of oliguria may also be congenital; temporarily it is

produced by the abstraction of water, after profuse sweats, or after diarrhœa.

Anuria, the uretha being pervious, can only occur in grave disorders of the kidney with uræmia; at other times it is found in strictures, calculi and neoplasms, as so-called *retention of urine.*

Having satisfied ourselves as to quantity, we seek to determine whether

2. The urine is indicative of a febrile state or not. From this we can frequently see whether the process is acute or chronic, the former being usually accompanied by higher degrees of fever.

The urine of *fever* is usually dark, reddish-yellow, concentrated, and diminished in volume. If the volume is increased rather than diminished, which rarely occurs, the coloring matter will, nevertheless, be found increased. With the nitric acid test, a distinct layer of the urates can always be detected.

In the presence of an acute exudative process, the urine, in the stage of exudation, is concentrated, acid, and contains many urates that come down, when cold, in the form of brick-dust sediment. Urea, the sulphates and the alkaline phosphates are increased, while the chlorides are diminished. The chlorides diminish with the increase of disease, and may be entirely absent.

In the stage of absorption, the concentration of the urine gradually diminishes, the reaction becomes neutral or alkaline (ammonium carbonate); the chlorides are again present in normal quantity, and urates (in the form of ammonium urate) and the

earthy phosphates are found in the sediment. At the same time the quantity of urine may be normal, or even diminished.

We can readily diagnosticate the febrile state, but can not diagnosticate the form of fever (except febrile diseases of the urinary apparatus). Even in diseases of the kidneys, we may err in that we may take an accompanying disease to be the principal affection. We examine, for instance, the urine of scarlatina. We find a febrile state, in addition, however, a desquamative or parenchymatous nephritis. As a result of the uroscopic developments we can only diagnosticate an acute nephritis, which evidently only accompanies the scarlatina, the latter not being detected by the analysis.

Differential diagnosis between different forms of fever, then, is impossible; but, nevertheless, we ought to examine the urine, as from it we can discover increase or diminution in the process, or other complications. The reappearance of the chlorides, for example, is considered a favorable sign, their disappearance, or the appearance of albumin, an unfavorable one.

Among the febrile processes there are some that require mention on account of their giving to the urine certain characteristic properties.

We find:

In jaundice, constituents of bile always present in the urine.

In mild jaundice (*icterus levis*) produced by absorption of bile, we find only a febrile state, and a goodly

quantity of biliary coloring matter; the chlorides are sometimes diminished.

In severer forms of jaundice produced by diseases of the liver (*icterus gravitis*), we find, besides great quantities of *urates* and *biliary coloring matter*, albumin and, sometimes, small quantities of *biliary* acid. The *chlorides* are usually absent.

In *acute yellow atrophy* of the liver we usually find an urine rich in biliary coloring matter, having a low sp. gr. and acid reaction. Urea is much diminished, and we find in its stead *leucin* and *tyrosin*. The chlorides disappear, and the urates and albumin are present, the latter in abundance. Even biliary acids may be detected in this urine. Great numbers of epithelial tubes and fibrin casts are found in this sediment, as well as epithelium from the kidney and blood corpuscles.

In *acute pulmonary affections* we find great quantities of urates. In diseases of the heart, or irregularities in circulation, we find stasis in the venous system, and, as a result, albuminuria (hyperæmic kidney).

In *peritonitis* we usually find large quantities of indican (Senator).

The urine of *meningitis* is usually very much concentrated, in proportion to the slowness of the pulse. As the differential diagnosis between typhus and meningitis is very difficult, frequently clinically impossible, the urine has been looked to for assistance. Unfortunately, this can not be relied upon. It is said that the urine of meningitis has a high specific gravity, a faintly acid reaction, and contains an in-

creased quantity of urates, besides a small amount of albumin. It is claimed, in addition, that when the urine of this disease is boiled, the earthy phosphates are precipitated without the addition of an alkali; the chlorides are always diminished. The urates are present; albumin may also be found in considerable quantity. At the same time the urine of typhus is said to have large quantities of ammonium in solution, although the reaction is acid. Much indican has been found in meningitis spinalis. In contradistinction to meningitis cerebralis, the sp. gr. is said to be diminished (Heller).

In *acute articular rheumatism*, in addition to high specific gravity, acid reaction, increase in urea and in urates, a great increase in the earthy phosphates is claimed as characteristic. The sediment contains pink urates and calcium oxalate colored by uroërythrin. If pericarditis sets in, the chlorides and earthy phosphates are rapidly diminished, but the uroërythrin becomes even better marked than before.

If the urine is not colored dark yellowish-red, and does not contain urates in large quantity, then we can assume that the disease is not accompanied with fever. For a few of those diseases that are without fever, therefore, principally chronic, characteristic properties of the urine have been described which are enumerated on account of completeness.

Chlorosis furnishes a very pale urine, of low sp. gr. corresponding with the diminished waste of tissue in the body. In hysteria the urine is similar, but the quantity is sometimes, and indican is always, increased

(*urina spastica*). Very pale urine is found, also, in hydruria and diabetes. In diabetes mellitus the sp. gr. is increased; usually there is found an increase in indican, and in the late stages of the disease, albumin is present. The other normal constituents are diminished in percentage, but increased absolutely (with the exception of uric acid). In diabetic urine, handsome yeast fungi, as well as networks of penicillium, are frequently found.

In *chronic diseases* of the *spinal cord* there occurs frequently a pale and light urine, which, in addition to much indican, and sometimes albumin, is said to contain sugar (?). Heller states that in the sediment he has frequently observed sarcina.

In *rickets* and *malacosteon* the earthy phosphates are very much increased, so that they form a heavy deposit.

In *diseases* of the *bones*, when they affect any great amount of osseous substance, the calcium salts are frequently found increased in the urine, in the form of the oxalate as well as the earthy phosphates, both in solution and in the sediment.

A very acid and concentrated urine is found in *chronic rheumatic arthritis*, depositing a copious sediment of urates and oxalate of lime. A decided increase in earthy phosphates is claimed as characteristic.

In *gout* the urine is similar to that of the above, only that uric acid is diminished in the urine and deposited in internal organs. Occasionally, however, a beautiful deposit of free uric acid is found.

In *intermittens*, during the chill, the urine is increased, pale and transparent; whilst it is dark during the period of fever.

In *chronic diseases of the liver*, notwithstanding the absence of fever, we find a dark, acid and concentrated urine. Biliary coloring matter that is not decomposed is rarely present. But we find the tests for normal coloring matter much increased — usually uroërythrin is present. The increase in these coloring matters is said to depend upon the presence of decomposed biliary coloring matter and increase in its excretion. The earthy phosphates are commonly diminished. In the sediment are found urates, and sometimes oxalate of calcium, both colored by uroërythrin. In *skin diseases* of a chronic nature, and especially in those in which a great area of skin becomes disabled for perspiration, we frequently find kidney disease as a complication, for instance, pemphigus, etc.

In *scorbutus* and *purpura hæmorrhagica*, hemorrhages from the kidney are not uncommon, as is also the case in *melanaemia*, where, in addition, parenchymatous disease of the kidney are found.

In *leucaemia* the urine is loaded with uric acid, lactic and hippuric acids also occurring.

CHAPTER VIII.

Diagnosis of Diseases of the Urinary Apparatus.

If we can prove the presence of albumin in urine which does not contain pus, blood, or any other albuminous fluid, then we have before us a case of *true albuminuria.* We are then dealing with a disease of the kidney. If blood and pus are present, and great quantities of albumin are detected, we are dealing with *mixed albuminuria* (Vogel). Great practice alone capacitates one for determining whether albumin is present in sufficiently large quantity to constitute mixed albuminuria. This can be acquired by mixing pus from wounds with normal urine, and then testing for albumin.

Microscopic and Chemical Aids to the Diagnosis of Various Forms of Albuminuria.

(*a*) true albuminuria.

1. *Hyperaemia of the Kidney.*

In active hyperaemia, which occurs after the imbibition of much fluid, no albumin is found. The quantity in twenty-four hours is very much increased, the color pale yellow, or even watery, the sp. gr. very low. Normal constituents are usually increased.

It is only after the kidneys have been over-exerted for some time, as in diabetes, that we find albumin

present in small quantity. It is also found in small quantities ($\frac{1}{10}\%$, usually less) in hyperaemic conditions of the kidney, which are caused by irritating substances excreted by the kidneys. For instance, after the continued administration of balsam copaibæ, turpentine, cubebs, corrosive sublimate, and other acrid remedies.

The changed chemical composition of the urine must also be considered as a cause for an irritated condition; *i. e.*, hyperaemia of the kidneys. It is a well-known fact, that highly concentrated, or very acid urine, can cause the most varied symptoms. Albumin is occasionally found in such urine, but it is usually transient.

Albumin can be detected in small quantity in oxaluria, and in the presence of large quantities of uric acid; partly on account of mechanical, and partly of chemical irritation, especially when the urine is very acid, and the crystals of uric acid are lance-shaped. In these cases, the internal administration of alkalies — excellent solvents for urates and oxalates — usually causes it to disappear. This form is not infrequently the first beginning of calculus of the kidney.

A transitory presence of albumin in small quantities is detected after convulsions, epileptic attacks, attacks of chills and fever, and in various forms of spasms of the blood-vessels. This is also frequently the case in acute febrile diseases (febrile albuminuria of Bartels), more especially so, in acute exanthemata, and not infrequently in other inflammatory affections of the

skin, as anthrax, furunculosis, erysipelas, after burns, etc. A parenchymatous affection is not uncommonly begun in hyperaemia, when the cause continues to act.

In passive hyperaemia, occurring as a result of stasis in the venous circulation, the albumin increases and diminishes with increase or diminution of pressure.

This form of kidney is most commonly found in valvular lesions of the heart that have not been compensated. Regulating the circulation by proper remedies, causes the albumin to disappear. The hyperaemic kidney is also found in chronic diseases of the lungs, notably in emphysema; furthermore, in tumors and exudations that prevent the flowing back of the venous blood; for example, large pleuritic exudations, ascites, ovarian tumors and pregnancy. In puerperal convulsions we do not always find the hyperaemic kidney (Rosenstein), but very frequently parenchymatous nephritis (Bartels).

As a result of marasmus and cachxia we also find this form of disease.

The urine, in simple hyperaemia of the kidney, is as follows: sp. gr. increased, but not always; the quantity either diminished or normal; reaction, acid.

Albumin present in small quantity ($\frac{1}{10}\%$ and below).

In the sediment are found either no organized elements, or blood corpuscles and epithelia from the straight uriniferous tubules. Hyaline casts hardly ever occur.

In febrile albuminuria the quantity of urates is increased, and that of the chlorides very much diminished.

In the hyperaemic kidney proper (stasis) the quantity is always diminished, sp. gr. high, color dark, and the reaction acid. The urine contains a large quantity of urates which frequently form large deposits, and make the urine very cloudy.

Albumin is present $\frac{1}{5}\%$ and above.

Hyaline casts and kidney epithelium are found in the sediment.

This form can be differentiated from parenchymatous nephritis by the absence of cellular elements (blood, lymph corpuscles and granular epithelium of the kidney) and granular casts in the sediment; from chronic interstitial nephritis and the amyloid kidney, by the dark color of the urine, its high sp. gr., its diminished quantity, and its richness in urates.

Parenchymatous Nephritis.

There are two forms of this disease; the acute and the chronic. The acute form is rarely primary, but developed from some other disease; the chronic is usually primary, and forms the second stage of what authors call Bright's disease.

(*a*) ACUTE PARENCHYMATOUS NEPHRITIS.

This, again, can be subdivided into its mild form, a so-called catarrh of the uriniferous tubules, or desquamative nephritis, and the real acute parenchymatous (diffuse or croupous) nephritis, the so-called Bright's disease.

(a) CATARRH OF THE URINIFEROUS TUBULES, OR DESQUAMATIVE NEPHRITIS,

Attacks, principally, the straight uriniferous tubules. The disease lasts from eight to fourteen days, or even less. The patients have little fever; they complain of pain in the limbs; weakness and pains in the back. Frequently the disease runs its course without compelling the patient to seek his bed. We rarely find œdema.

The urine presents the following changes:

The quantity is either normal or slightly diminished, the same is true of the sp. gr. The color of the urine is wine-yellow, rarely yellow; the reaction acid. It is always cloudy from admixture of cellular elements, and frequently deposits a dense sediment.

The normal constituents are unaltered. Of abnormal substances albumin is found in $\frac{1}{10}$–$\frac{1}{5}$ %, and traces of blood-coloring matter.

The sediment is principally made up of an increased mucous secretion. With the microscope we find numerous epithelial cells from the straight tubules, usually little altered, but sometimes colored brownish by the blood-coloring matter. They frequently adhere to each other, forming epithelial tubes, or they stick to hyaline casts, forming epithelial casts. Single hyaline casts are also found, as well as red blood corpuscles and lymph corpuscles in great numbers.

Catarrh of the uriniferous tubules develops as a morbid reaction, after the introduction of instruments

into the bladder, after catheterization of a sensitive bladder, the dilation of strictures, lithotripsy, etc.; in addition to this, after acute inflammatory processes, especially upon the skin, exanthemata. It may also develop ex-contiguo from acute cystitis after gonorrhœa.

(β) ACUTE PARENCHYMATOUS NEPHRITIS PROPER.

This process may be ushered in by very turbulent symptoms, or may occur without marked subjective symptoms, the latter occurring in cachectic, reduced individuals.

Dropsy is the first symptom that causes uneasiness to patient and physician. It appears as the characteristic œdema of the eyelids and face. Severe cases are accompanied by anuria and convulsions. The smaller the quantity of urine in twenty-four hours, the more intense is the attack, so that anuria lasting for some time nearly always results fatally.

We find the urine as follows:

The quantity is very much diminished, sometimes 250 c. c. Sp. gr. is usually increased, the reaction acid, the color brownish-yellow and very turbid, frequently having a large deposit of cellular elements.

The normal constituents are diminished.

Of abnormal substances we find large quantities of serum-albumin and blood-coloring matter; the quantity of the former varying from 1, 5 to 6 per cent., so that the urine solidifies upon boiling.

The sediment is usually of a brownish color, and consists, principally, of coarse, sometimes long or

spiral, casts of fibrin, colored by the blood-coloring matter. These sometimes contain a great number of white or red blood corpuscles (blood casts), or brown epithelial cells of the uriniferous tubules (hemorrhagic). In other cases only debris of cells is found, surrounding the nuclei and adhering to or imbedded in the substance of the casts. In addition to this, we find cells from the tubules, many blood and lymph corpuscles and much detritus, colored brown by the blood-coloring matter.

This form is either a primary disease or a sequela to another acute disease. It is very frequent after the acute exanthemata, especially after scarlatina; also after diphtheria, relapsing fever, phlegmonous inflammations, erysipelas and carbuncles; after the administration of preparations made from cantharides (cantharidin), as well as after the internal use of caustic remedies (corrosive sublimate). It is frequently observed after catching cold; after burns, inflammatory rheumatism, and cholera, and it is not uncommon during pregnancy. It also develops during the course of chronic parenchymatous nephritis.

The prognosis is usually favorable, but death may ensue from acute uræma, or the form may be changed to a chronic inflammation.

(γ) CHRONIC PARENCHYMATOUS NEPHRITIS.

Dropsy is the first symptom in this form also. Fever is absent.

The urine shows the following changes:

As long as the disease continues to progress, and

during its acme, the quantity is diminished; as soon as the inflammation recedes, the quantity increases, and in the stage of atrophy may be very much increased. Its color is yellowish, often brownish-yellow; it is turbid from cellular elements, which form an appreciable sediment. The reaction is acid, and the sp. gr. usually diminished. Normal constituents, especially urea, are frequently diminished.

Albumin is found in considerable quantity ($\frac{1}{2}$ to 1 to 2%), and blood-coloring matter can usually be detected.

In the sediment are found dark, granular casts, also half granular casts, *i. e.*, those that are granular in spots, the rest of the cast being made up of hyaline substance; granular epithelium of the kidney, red and white blood corpuscles and molecular detritus.

In the stage of secondary atrophy, the quantity is very much increased, the sp. gr. very much diminished, the color pale yellow, the urine turbid and having an appreciable sediment. When atrophy affects both kidneys, the excretion of normal constituents, especially of urea, is very much diminished. Albumin is present in small quantity, $\frac{1}{10}$ to $\frac{1}{5}$ %. In the sediment, granular masses of detritus, granular epithelium of the kidney and fragments of granular casts are found.

Only in the minority of cases does this form arise from the acute form; it generally runs its course insidiously. It most frequently arises from the acute form, after scarlatina and rheumatic processes, after

profuse suppuration in the bones, and also from nephritis of pregnancy.

The form that is chronic from the beginning, frequently develops from purulent processes in bone and joints, as a result of syphilis, phthisis, malaria, scrofulosis and cachexia. Intemperance is also considered as cause.

The prognosis is not very favorable. Cases occur in which, after dropsy and albuminuria has lasted for years, health is regained; but these are exceptions. After syphilis and malaria, as well as after osseous suppuration, a cure can sometimes be affected by the proper remedies.

5.—Interstitial Nephritis.

The small amount of interstitial connective tissue present in the kidney may be subjected to hyperplastic proliferation or to destruction by suppuration. As a result we have two forms of interstitial nephritis: the hyperplastic and the purulent.

(*a*) HYPERPLASTIC INTERSTITIAL NEPHRITIS—CIRRHOSIS OF THE KIDNEY—CONTRACTED KIDNEY PROPER.

This disease rarely occurs in the young, most commonly in the old.

It may exist for a long time, and have reached full development, without calling attention to its existence by symptoms of any kind. Dropsy rarely sets in, and when it does, only in the last stage.

A bounding pulse of high tension, and an enlarge-

ment of the left ventricle of the heart, are its usual symptoms.

Disturbance of sight is the most common complication of this disease, and is frequently the first symptom which forces a patient to seek help.

We find the urine as follows:

Its external appearance is that of normal urine; clear, transparent, of a wine-yellow color. In quantity it is usually increased, but polyuria is not always the rule. The sp. gr. is either normal, or, more commonly, reduced; the reaction is acid.

The normal constituents are, as a rule, unaltered.

Albumin is found in moderate quantity ($\frac{1}{10}$ to $\frac{1}{2}$ %). It may disappear entirely, especially when the patient is confined to bed, for which reason we find much less albumin in the morning urine than in that which is passed during the day.

Macroscopically, no sediment can be observed. Even with the microscope, we frequently fail to find anything abnormal. Only after careful and repeated examinations do we find a single hyaline cast, a blood corpuscle, or epithelium from the kidney.

The prognosis, when diagnosis has been established, is usually unfavorable, but the course may be very long.

The etiology is, as yet, dark.

(b) SUPPURATIVE INTERSTITIAL NEPHRITIS.

This form may be of traumatic, idiopathic, pyaemic or metastatic origin. It frequently originates in chronic pyelitis, as the disease of the pelvis spreads to the con-

nective tissue of the kidney and causes suppuration. This form is the usual termination of cases in which there has been surgical interference with the urinary organs. For instance, after catheterization of a paralytic bladder, after forcible dilatation of strictures, after lithotripsy, suppurative nephritis sets in.

To this form, therefore, the name of "the surgical kidney" was formerly given.

Calculus of the kidney predisposes to this form, complicated by large abcesses of the kidney and pyonephrosis.

We find the urine of the following description:

Its color is yellow; it is turbid and scanty; its smell is frequently fecal; sp. gr. diminished, and reaction either neutral or alkaline.

The normal constituents, especially urea, are diminished.

Albumin is present in considerable quantity ($\frac{1}{2}$ to 1 %). Blood-coloring matter is also present; we not infrequently find large quantities of ammonium carbonate and sulphide.

The sediment is copious, and consists principally of pus, mixed with blood in greater or less quantity. Microscopically, numerous bacteria, molecular detritus and epithelia from the kidney, and thick, dentritic casts made up of bacteria, are found (*Pyelo-nephritis parasitica*—Klebs).

If complicated by parenchymatous nephritis we also find dark, granular, thick casts, coming from the straight uriniferous tubules.

The course of the disease is usually acute, and the

termination, death. In chronic cases the larger abcesses break into the pelvis.

Kidney abcesses can only be diagnosticated by means of determining the quantity of pus discharged—easily accomplished by collecting the urine in appropriate vessels. Pus which appears and disappears suddenly, with the microscopic signs of necrotic kidney-tissue (glomeruli and uriniferous tubules), are the best indications of the existence of an abcess.

4.—The Amyloid Kidney.

Amyloid degeneration of the kidney is usually the symptom of a constitutional disorder. It occurs in profuse suppuration of bone, as well as in other suppurative processes which last for a considerable length of time. In pyonephrosis of one side, the other kidney frequently becomes amyloid. Scrofulosis, chronic tuberculosis, syphilis and malaria, favor the development of this form of disease. It is occasionally found idiopathically.

Amyloid kidney, complicated by parenchymatous nephritis, is of frequent occurrence.

This degeneration develops without producing any important symptoms, but it may be laid down as a rule, that an amyloid kidney always secretes more urine in twenty-four hours than a normal one. The quantity never becomes so great, however, as in atrophy of the kidney.

The urine is pale yellow, clear, has a low sp. gr., an acid reaction, and is without microscopic sediment.

The normal constituents are usually diminished.

Serum-albumin is constantly found in moderate quantity (from $\frac{1}{10}$ to 1 or 2 %). A considerable amount of globulin is also found (Senator, Edlefsen), which may be looked upon as characteristic of this form of disease.

There are frequently no cellular elements to be found in the sediment, but delicate hyaline, or waxy, shining, yellowish casts sometimes occur. Amyloid epithelium of the kidney is more rarely observed, and, in common with the casts, changes to a mahogany color upon the addition of an aqueous solution of iodine, and upon the further addition of sulphuric acid, becomes violet. In the uncomplicated amyloid kidney, blood is not found in the sediment.

The prognosis depends upon the disease at the bottom of the kidney disease. In syphilis and malaria we will, therefore, have the best results.

In the differential diagnosis of the various forms of true albuminuria, the following additional points must be taken into consideration:

1. If we find a sediment which can be detected with the microscope, and is made up of cellular elements (blood, pus corpuscle, casts, etc.), we have either a parenchymatous nephritis or an interstitial suppurative nephritis.

a. In parenchymatous nephritis we find epithelial, fibrin and granular casts, kidney epithelium, blood, and lymph corpuscles.

b. In suppurative interstitial nephritis we find pus and blood corpuscles, bacteria, sometimes casts of bacteria, or short and thick, dark, granular casts.

2. If the urine is clear, or cloudy with urates, and we find no sediment of cellular elements, then we either have an hyperaemic kidney, an hyperplastic interstitial nephritis, or an amyloid kidney.

a. The hyperaemic kidney can be differentiated from the other two by the diminished quantity of urine, by its dark color, its high sp. gr., and frequently by the abundance of urates it contains.

b. The amyloid kidney, by its having globulin and waxy casts, and amyloid kidney epithelium.

Clinically, we find dropsy in amyloid degeneration (as well as in parenchymatous nephritis), while in true atrophy this is the exception, and only occurs late in the disease.

c. In true atrophy we find hypertrophy of the heart and a bounding pulse, neither of which occur in parenchymatous nephritis and amyloid kidney. In the amyloid kidney we find enlargement of the liver and spleen (amyloid degeneration).

(*b*) Forms of Mixed Albuminuria.

It is a characteristic of mixed albuminuria that the urine contains more albumin than is called for by the pus present in the sediment. It includes those diseases of the pelvis of the kidney which, when advanced, attack the kidney itself, and complicate pyorrhea with true albuminuria.

As a proof that the papillary portion of the kidney is also affected in the pyelitic process, observe the occurrence of kidney epithelium in the sediment;

also, that after the process has continued for some time, the pelvis is dilated at the cost of the papillary portion, which has been more or less consumed.

1.—Pyelitis.

Pyelitis frequently accompanies acute febrile diseases, parenchymatous nephritis, and the later stages of diabetes mellitus. The use of cubebs, copaiva, etc., is sometimes followed by this form of disease. Renal calculi, parasites, tumors and tuberculosis in the pelvis, are almost always accompanied by it. Ex-contiguo, it or pyelo-nephritis develops from stasis of urine, as we find in hypertrophy of the prostate, paralysis of the bladder, strictures of the urethra etc. Pyelitis is produced, also, by compression of the ureters by tumors, exudations, and by the retroflexed or gravid uterus, and also occurs after gonorrhœa, mechanical irritations of the neck of the bladder, and of the bladder itself, by surgical instruments, etc.

Two forms of pyelitis are distinguished, the acute and the chronic. We frequently have points offered us for the diagnosis of pyelitis calculosa and tuberculosa in the sediment.

Croupous and diptheritic pyelitis are usually caused by such grave diseases that their own symptoms are pushed into the background.

(*a*) Acute Pyelitis.

The best type of this disease is found after surgical interference with the urinary organs; in the course of

acute inflammatory affections, and after gonorrhœa. Its urine is moderately diminished in quantity, it is dark, cloudy, has a high sp. gr., and is of acid reaction. After standing, an appreciable deposit is found. Normal constituents unchanged, except in the presence of fever, when an increase of urates and diminution of chlorides will be observed.

Albumin is always present in greater quantity than would correspond with the comparatively small sediment of pus ($\frac{1}{10}-\frac{1}{2}$ %). Blood-coloring matter is not constant, and when present, only in small quantity.

The sediment is chiefly made up of mucus, mixed with more or less pus. The pus cells are round, and frequently many of them are united to form an oval or cylindrical plug. These come from the papillæ, and frequently contain epithelium. We always find blood corpuscles; epithelium from the papillary portion of the kidney, of an oval or pear-shape form, is found in great abundance. Frequently two or three epithelial cells still cohere. Sometimes we find the epithelial cells tinged by blood-coloring matter.

Epithelial cells with one or two processes, arranged like shingles, usually called epithelium from the pelvis, is not at all characteristic for pyelitis. Indeed, this epithelium from the pelvis can hardly be distinguished from that of the bladder. Besides, these cells are not always found in pyelitis, therefore the epithelium from the papillary portion of the kidney alone is characteristic for this form of inflammation.

In acute pyelitis, epithelium from the kidney is always found in great abundance (ten cells, and over,

in one field); in chronic pyelitis, on the other hand, it is not very abundant.

Acute pyelitis, when the result of surgical interference, of acute inflammatory processes or gonorrhœa, usually allows of a favorable prognosis, in that a few weeks are sufficient to affect a cure. Sometimes the acute form becomes

(*b*) Chronic Pyelitis.

In chronic pyelitis the quantity of urine passed in twenty-four hours is always increased, so that polyuria may be put down as a characteristic sign of this disease. In severe cases, the quantity averages from five to six litres. The color of the turbid urine is pale reddish-yellow, sometimes a slight greenish shade. The sp. gr. is always diminished, and the reaction acid. The deposit corresponds with the amount of pus present.

Albumin is always found in larger quantity than could be expected from the amount of pus present ($\frac{1}{10}-\frac{1}{2}$ %). Blood-coloring matter is always present. The sediment has a greenish-yellow color, is flaky, does not adhere to the vessel, and consists chiefly of pus. The pus cells are, not infrequently, forked and branched, in contradistinction to other purulent processes in the urinary organs. They also form round, oval, or large plugs (from the ductus papillaris), which are characteristic of chronic pyelitis.

Epithelia are found in small number, and when suppuration is profuse they are entirely absent, prob-

ably because they become pus cells by endogenous growth.

Blood corpuscles are not found in ordinary chronic pyelitis, but when the disease is the result of renal calculi, tuberculosis, tumors, or entozoa, they are never absent.

The prognosis is rarely favorable. With us, it is usually a complication with the formation of calculi. The termination in pyonephrosis, then perinephritis and external escape of pus, or occasionally into the intestine or bladder, is not uncommon, and usually occurs in young and healthy individuals. In weak patients the pyelitis becomes interstitial nephritis, which finally terminates in chronic uræmia.

(*c*) Pyelitis Calculosa.

Real calculi are principally formed by the deposit of uric acid in the kidney or pelvis, and the stones which pass spontaneously are consequently of a yellowish-brown color, and made up of uric acid or urates. After hemorrhage or long-continued suppuration, by the deposit of the earthy phosphates, we also have cystin (very rare) and the so-called secondary formation, as the origin of renal calculi. Calcium oxalate is rarely the primary deposit, but frequently forms layers.

The most common cause for the formation of renal calculi is the deposit of uric acid, on account of its absolute or comparative excess. This deposit is favored by the acidity of the urine, which increases

with its concentration, producing those rough crystals of uric acid which nearly always form the nucleus of these calculi. The predisposition to calculi is to be sought for in concentrated, highly acid urine, rich in uric acid, especially when it crystallizes in the rough or lance-shaped crystals.

The beginning of this disease can be diagnosticated when we find, besides the properties of the urine already enumerated, mild albuminuria (hyperaemia of the kidney) and single blood corpuscles in the sediment. The albuminuria is only temporary, and appears when the urine is either very much concentrated or contains a great excess of uric acid.

The presence of large concretions can be diagnosticated by the occurrence of parenchymatous hemorrhages. The urine is reddish-brown, or coffee-colored, especially after bodily exercise.

If the calculi are not passed, then there arises pyelitis—*pyelitis calculosa.*

This may be found either in a mild or severe form.

The mild form occurs with calculi of small diameters, and frequently has characteristic elements in the sediment, whilst the severe form can only be differentiated from chronic pyelitis by the presence of blood corpuscles in the sediment. The latter form is usually observed with large calculi, forming a focus for pyonephrosis, paranephritis, and emptying of the pus.

The milder form shows the following changes in the urine: The quantity is usually normal, sometimes diminished, never increased; the color dark, the sp.

gr. normal or increased; the reaction is very acid, and there is frequently a considerable sediment.

Uric acid is present in excess in the sediment, and a layer of urates is to be detected by the nitric acid test.

Albumin is found from $\frac{1}{10}$ to $\frac{1}{2}$ %, always in greater quantity than would correspond to the amount of pus. Blood-coloring matter is always present, even though sometimes in small quantities.

The sediment consists, chiefly, of lance-shaped uric acid crystals (cystin and calcium oxalate), mixed with curdled pus. We also find numerous red blood corpuscles (especially microcytes) and epithelia from the kidney.

Diagnosis is made positive by the clinical signs, and by the absence of calculi upon sounding the bladder.

Renal calculi only offer a favorable prognosis when small. When they are large, or branched, the prognosis must be unfavorable, or, at least, doubtful. The greater the suppuration, and the longer its duration, the less favorable does the prognosis become.

The disease is usually unilateral.

(*d*) Pyelitis Tuberculosa.

Pyelitis tuberculosa is, as a rule, a symptom of general tuberculosis, or tuberculosis of the uro-genital apparatus. For this reason, we frequently find it complicated by chronic parenchymatous affections of the kidney (nephrophthisis — nephritis ulcerosa). In cases in which tuberculosis of the pelvis and kidney,

both, exist, we find large, waxy casts, much molecular detritus, pus and blood corpuscles, and kidney epithelium, in the sediment. A great quantity of albumin is found in the urine.

Simple pyelitis tuberculosa, on the other hand, produces the following changes:

The quantity of urine is not increased very much; its color is yellow, frequently brownish-red (on account of the admixture of blood). It is always cloudy, has a normal or diminished sp. gr., and an acid reaction. The sediment is grayish or brownish, and flocculent.

The excretion of the normal constituents is not very much changed.

Albumin is found in from $\frac{1}{10}$ to $\frac{1}{2}$ %. Blood-coloring matter can always be detected.

The sediment consists of pus, principally, and a small quantity of blood; in addition, we find kidney epithelia and molecular detritus, mixed with bacteria, the latter united so as to form spherical or cylindrical bodies.

The presence of blood corpuscles usually denotes an ulcerative process in the pelvis, and will, therefore, be observed both in the urine passed during the day and during the night; in pyelitis calculosa, on the other hand, the urine passed in the morning, or whilst the patient is at rest, contains much less blood than that passed during the day, or after exercise. In tubercular pyelitis the desire to pass water is not accompanied with as much pain, and is not so frequent, as in calculus-pyelitis. In addition, the usual symptoms of lithiasis are absent.

The diagnosis is much easier if we find hard, plastic exudations in the testicles, scrofulous cicatrices, enlargement of glands, other diseased processes in bone, deep fistulæ in ano, etc.

When general tuberculosis is present, the prognosis must be unfavorable. In tuberculosis of the genital organs, when it affects young and healthy individuals, improvement or comparative health may be secured; for example, after the removal of a tubercular testicle.

NOTE.—The brilliant discovery of Koch makes the diagnosis of all tubercular processes a comparatively easy one. In pyelitis the sediment is examined for the presence of the bacillus of tuberculosis; it is carefully collected by decanting the urine, and then a small quantity taken, spread out upon a slide, or rubbed between two thin covers. The thin layers are then carefully dried, and the coloring matter applied to them. For the purpose of staining the bacilli, there are several that may be used; the original method of Koch, slow but sure, or one of the modifications to insure rapidity. The method most convenient to the clinician and practicing physician is carried out by taking aniline oil, heating this in a test-tube until it has cleared up, and then adding an alcoholic solution of fuchsin until a rich red color is produced. This fluid is then poured upon the thin layer of sediment and allowed to stand for from fifteen to forty-five minutes—or the thin cover may be floated upon a watch-glass containing the aliline oil and fuchsin. The longer the exposure to the action of the fluid, the more positive are we concerning the result. After the staining has been effected, the slide or thin cover is washed with distilled water, put into a 33% aqueous dilution of HNO_3, and decolorization of the stained spot then proceeded with. This completed, we again wash with distilled water, and then mount in glycerine and

examine, if possible, with a homogeneous lense and a condenser. The ordinary high powers, however, are sufficient for the detection of the bacillus, especially to one experienced, yet it is always safer to examine with the combinations recommended by Koch.

In *echinococci* we sometimes find pyelitis, which, however, is not to be distinguished from any ordinary pyelitis. It is only when the tumor has emptied into the pelvis that we find the characteristic cysts in the sediment, as well as single scolices with a double row of hooklets, or remnants of them, and single hooklets.

In *bilharzia haematobia*, pyelitis accompanies cystitis, and is always complicated by copious parenchymatous hemorrhages. Numerous blood and pus corpuscles, kidney and bladder epithelia, and fibrin coagula, enclosing the characteristic ova of the bilharzia, are found in the sediment. Large quantities of albumin and blood-coloring matter are present in solution.

Para- or *perinephritis* can not be diagnosticated from their urine, as the latter, even in a severe attack, frequently produces a normal urine.

2.—HÆMATURIA.

Strictly speaking, this is a symptom, not a disease, but as it accompanies so many diseases, and as these diseases can not always be determined, we have to be satisfied with the diagnosis, "hæmaturia from unknown causes." For this reason we have thought best to treat of it here.

Hemorrhages from the urinary apparatus may be divided into three classes:

a. Hæmoglobinuria (hæmatinuria of Vogel);

b. Parenchymatous hemorrhage, and

c. Copious hemorrhage, produced by the rupture of large blood-vessels.

1. Hæmoglobinuria is characterized by a reddish-brown, brownish-black urine, from which, even after it has stood for hours, no red deposit forms. It retains its uniformly reddish-brown color, because the blood-coloring matter is dissolved. The reaction is usually acid, and sp. gr. diminished. It contains much hæmoglobin and methæmoglobin. In the sediment, hemorrhagic epithelia and brown molecular detritus are sometimes found. Blood corpuscles are not present.

2. In *parenchymatous* hemorrhage we also observe a reddish-brown, frequently coffee-colored urine, which will retain its color for a long time, but deposits a reddish-brown sediment, consisting of red blood corpuscles. Its reaction is acid, its sp. gr. varies, and it holds hæmoglobin (more or less altered) in solution.

For the parenchymatous hemorrhage, the sediment is characteristic. Blood corpuscles of various sizes are found in it. The round, normal corpuscles, with depressions, are frequently not to be found in it at all, but they appear, instead, globular, spherical, and colored brown. They are often entirely colorless, and of a ring-like appearance. Very large corpuscles, corpuscles of one-fourth the normal size, and some as small as specks of dust, are seen in one and the same field.

These microcytes, which have so frequently, in modern times, been observed in the blood of patients, were long since known to exist in urine from parenchymatous hemorrhage, and were considered characteristic of it.

3. In the hemorrhage coming from the *rupture of large vessels*, the urine is either dark reddish-yellow or red, similar to venous blood. The reaction is, commonly, neutral or alkaline. The sp. gr. varies. The urine usually contains traces of coloring matter in solution; it is only when much ammonium carbonate is present, a rare occurrence, that considerable quantities are dissolved.

Usually, the urine from rupture of large vessels deposits all its blood, after standing for several hours, in the form of a copious red sediment, in which the blood corpuscles appear of their normal color, size and shape.

Albumin can always be found in this kind of urine.

These three forms of hemorrhage may originate in the bladder, the pelvis, or the kidney, and we are not always so fortunate as to be able to state where the blood comes from.

1. We seek to utilize the reaction for differential diagnosis. It is generally accepted that in hemorrhage from the kidney it is acid; from the bladder, alkaline. But this is not always the case; indeed, the one can only occur when hemorrhage is complicated by purulent catarrh of the pelvis or bladder. Here the reaction on litmus is not decisive, for, in large hemorrhages, we find the alkalinity of the blood neutralizing

the acidity of the urine, and we may have an alkaline reaction even if the blood comes from the kidney. The internal administration of alkalies might be sufficient to make the urine alkaline, or the amount of pus formed in the pelvis of the kidney, with its alkaline reaction, might be sufficient to neutralize the urine — in these cases we would have an alkaline reaction, and yet the hemorrhage not from the bladder.

On the other hand, it can not be denied that hemorrhages occur from the bladder in which the reaction of the urine is acid. This is always the case, when there is no purulent catarrh of the bladder, and when the hemorrhage is not very great.

Of greater importance than the reaction, is the detection of ammonium carbonate. When this is present in large quantity, the likelihood of hemorrhage from the bladder is greater, more especially if we find crystals of the triple phosphate in the sediment at the same time.

2. The color of the urine is of very great importance in this respect. The older practitioners have always associated its reddish-brown or brownish-black color with hemorrhage from the kidney, and the light red with hemorrhage from the bladder. This is not altogether correct. The dark colors are produced by decomposed hæmoglobin (methæmoglobin), and can only occur when blood has been intimately mixed with urine and retained within the body for some time. This is the case in parenchymatous hemorrhages, where the blood is gradually mixed with the

urine, and the blood corpuscles remain a long time in a comparatively large quantity of fluid containing substances which are undergoing a retrograde metamorphosis; the constituents of the urine have time to exert their destructive influence upon the red corpuscles, converting the hæmoglobin into brown methæmoglobin.

For this reason the urine in parenchymatous hemorrhages, even in such as come from the bladder (cancer), takes brown tints upon itself.

It is an entirely different matter when hemorrhage is produced by the rupture of larger vessels (hæmorrhoids of the bladder). Here a large quantity of blood is suddenly introduced into the bladder, and as suddenly dilates it. This is followed by tenesmus, and the blood is passed before the urine has had time to act upon the hæmoglobin.

As hemorrhages from the bladder are produced, as a rule, by rupture of large vessels, and those from the kidney are parenchymatous, we can readily understand how the different color of urine becomes a very valuable diagnostic point.

3. The specific gravity is of importance in that in hemorrhage from the kidney or pelvis, some disease is usually present which produces polyuria, therefore low sp. gr.; while in hemorrhages from the bladder there is, as a rule, no change in this respect.

4. If *coagula* are present they sometimes point positively to the seat of the lesion.

If the coagula are soft and have the color and consistency of fresh, coagulated blood, they have not

existed for a long time; but if they are discolored, they are old, and have been retained for some time. Short, rod-like coagula sometimes come from the dilated pelvis (Simon), and are found after hemorrhages from the kidney; they were formerly considered as concrements made up of pure fibrin (Heller).

Large, irregular, shred-like coagula are said to come from the bladder. We must call especial attention to the fact that the rod-like coagula alone can be considered of diagnostic value. If they are present we can state positively that the seat of hemorrhage is above the ureters, for the long coagula are molds of the ureters. The irregular coagula, on the other hand, are not all characteristic. They may be produced in the pelvis as well as in the bladder.

It may even happen that fluid blood, poured out in the kidney, passes into the bladder and coagulates there.

Moreover, coagula are not constant in hemorrhages. Parenchymatous and copious hemorrhage will rarely produce them. They occur when the blood comes from vessels of smaller calibre.

5. The most important of all the aids to diagnosis is microscopic examination of the sediment.

The so-called blood casts and hemorrhagic epithelium of the kidney are characteristic of parenchymatous hemorrhages from the kidney. They are not found, however, after copious hemorrhages from larger vessels. It is highly probable that kidney epithelia are present, but they are covered over by the great numbers of blood corpuscles, and can not be detected.

Hemorrhages from the bladder are frequently not at all characterized by the sediment. We sometimes find an increase of epithelia from the bladder, and crystals of triple phosphate.

After this description of the micro-chemical characteristics of hemorrhages from the urinary apparatus, we will proceed to discuss the diseases in which they occur, and, at the same time, seek new diagnostic points.

I. *Hæmoglobinuria* (with or without methæmoglobinuria) occurs in hemorrhagic diathesis, scorbutus, congestive chills, in putrid typhus fevers, and, in fact, in all diseases which are accompanied by blood dissolution; after the inhalation of arseniuretted hydrogen, carbonic acid gas, and other similar substances. We also find hæmoglobinuria after transfusion with animal blood, especially in cases where much blood has been used.

II. *Parenchymatous Hemorrhages* may come from any part of the urinary apparatus.

a. In addition to the diseases already enumerated, hemorrhages are found from the kidney, usually associated with hæmoglobinuria; also:

1. Occasionally, in acute febrile diseases, especially in the exanthemata, where the hemorrhage represents a higher degree of hyperaemia.

2. In the majority of cases of chronic parenchymatous nephritis.

3. As a rule, in atheromatous degeneration of the vessels of the kidney.

4. In thrombosis of the renal vein, occurring in

general cachectic conditions; in puerperal fever, with phlebitis of the femoral and uterine veins; furthermore, accompanying serious injuries of the kidney, sometimes with traumatic nephritis; finally, as a result of compression by tumors in the neighborhood of the hilus.

Thrombosis of the renal veins sometimes occurs in infants suffering with intestinal catarrh. According to O. Pollak this may be recognized as follows: The child becomes jaundiced, a great diminution of urine follows, and the sediment contains blood casts, blood corpuscles, and hemorrhagic kidney epithelium.

Hemorrhages from the kidney are furthermore observed:

5. Constantly in renal calculi, when severe pyelitis has not developed. Besides the elements which are characteristic of calculi, the sediment contains blood corpuscles and kidney epithelia.

6. In cancer of the kidney, where nothing suspicious is found but the hemorrhage. We have never found cancer cells or tissue in the sediment, but it may occur when the cancer grows into the pelvis of the kidney.

In small children, large tumors, the size of a fist, are found in the kidney, without one being able to detect a sign of albuminuria. Hæmaturia, therefore, is not always present in tumors of the kidney, but is a very common symptom.

7. In nephrophthisis or in caseous inflammation of the kidney, of the pelvis, and the ureters. In addition to the microcytes, we find in the sediment, kidney epithelium, pus cells, much molecular detritus,

numerous vibriones and cocci; sometimes, waxy casts, mixed with casts made up of bacteria.

b. Hemorrhages from the bladder are observed:

1. In stone in the bladder and in catarrhal ulcers at the neck of the bladder. Hæmaturia is of a mild nature.

But in both cases microcytes can not be detected in the sediment. All the red corpuscles are of normal size. If catarrh of the bladder is also present we find its characteristic urine.

Hæmaturia in vesical calculus becomes more intense after exercise, and ceases when the patient is in bed. Hæmaturia in catarrhal ulcers, situated at the neck of the bladder, usually originating in gonorrhœa, takes place at the end of micturition, when the sphincter of the bladder begins to contract.

2. In papilloma and villous carcinoma of the bladder, parenchymatous hemorrhages also arise from the papillomatous proliferations of its mucous membrane. Not infrequently, we find in the sediment necrotic papilla tissue, which facilitates diagnosis. (See chapter on cancer.)

c. Parenchymatous hemorrhages throughout the entire apparatus occur.

1. Sometimes, after the emptying of a paretic or paralyzed bladder with the catheter. If the entire urine is drawn off, a quantity of which probably has remained for years in the bladder, because the paretic bladder was unable to pass it, an hyperaemia ex-vacuo must occur, which becomes the more intense the thicker the muscular coat of the bladder, and the

greater its inability for contraction. At the same time the pressure in the kidney is also changed, producing a parenchymatous hemorrhage.

2. They are also observed in Egypt, as a result of the bilharzia hæmatobia. Emboli of the vessels of the mucous membrane are produced by the ova of the distoma hæmatobium. The sediment is characteristic for this disease.

III. *Large hemorrhages after the rupture of vessels* only occur in tumors and varicose vessels at the neck of the bladder.

In tumors they only occur when the cancer has existed for a long time and begins to ulcerate. In the so-called hæmorrhoids of the bladder, the bleeding is very profuse, coming on very suddenly and, after one or two days, rendering the patients very anaemic. It usually lasts for several days, then leaves the patient perfectly well, returning after months or years. In the sediment we only find blood corpuscles of normal size.

In diphtheritic and croupous processes of the bladder, occurring after dissolution of the blood, we also find blood in the fetid, ichorous and alkaline urine.

3.—Cysto-Pyelitis and Pyelo-Cystitis.

Under this designation, a purulent catarrh, which affects pelvis, ureters and bladder, is understood. If the pelvis is principally affected it is cysto-pyelitis, but if it is the bladder, then we term it pyelo-cystitis.

We determine by characteristic signs whether the bladder or pelvis is most affected.

If pyelitis prevails, polyuria will usually be present; the urine will be of neutral or faintly alkaline reaction; sp. gr. low, and the purulent sediment will not adhere to the glass. Albumin will be present in greater quantity than is proportionate to the pus, and in the sediment, pus corpuscles, kidney and bladder epithelium, and crystals of the triple phosphate will be found. The pus corpuscles are well preserved, and occasionally united into plugs.

If cystitis prevails, polyuria is absent; the urine is very alkaline, its sp. gr. normal, or only slightly diminished. The sediment is pasty, and adheres to the vessel. Albumin is present in quantity corresponding with mixed albuminuria, and considerable quantities of ammonium carbonate can be detected.

The pus corpuscles in the sediment are very much swollen, and lie between great numbers of the triple phosphate crystals; the sediment also contains single kidney and bladder epithelia.

Cysto-pyelitis and pyelo-cystitis frequently occur in stricture of the urethra, in hypertrophy of the prostate, and in paresis or paralysis of the bladder.

Cysto-pyelitis and pyelo-cystitis may easily originate from cystitis or pyelitis, by direct continuity of the tissues. It is not rare for cystitis to alternate with pyelo-cystitis, and pyelitis with cysto-pyelitis.

Prognosis depends upon the cause and prevailing disease.

(*c*) Forms of False Albuminuria.

False albuminuria is distinguished from the other forms by the fact that true albumin is present in

quantities which correspond with the quantity of blood or pus present in the urine. The albumin which is found is from pus and blood serum, and when these disappear suddenly, as after the rupture of an abcess or varix into the bladder, the albumin will disappear also.

We have seen the derivation of true and mixed albuminuria, and can arrive at the seat of lesion producing false albuminuria by exclusion: the bladder, urethra, and their adnexa.

1.—Cystitis—Catarrh of the Bladder.

Cystitis exists in two forms, the acute and the chronic, each of which has three degrees.

In cystitis of the first degree, urine contains neither pus nor albumin, but simply an increased amount of mucus, and has an acid reaction. In the second degree it contains albumin and pus, has an alkaline reaction, and a greenish, mucilaginous sediment. The third degree is characterized by ichorous, fetid urine, much albumin, pus and blood, and a marked alkaline reaction; it is the result of ulcerative processes in the bladder, and is not infrequently accompanied by suppurative nephritis.

Urine usually has an alkaline reaction, in catarrh of the bladder, and many practitioners, even to-day, diagnosticate this form of disease by means of litmus paper. This test is usually reliable, but there are cases of cystitis in which the urine has an acid reaction. This is only the case, however, with urine

which has been recently passed, as it becomes alkaline after standing a few hours.

(*a*) *Acute Catarrh of the bladder of the first degree* presents the following peculiarities:

The quantity of urine is not diminished. The urine has a normal or dark wine-yellow color, and is turbid. The reaction is faintly acid, but changes in a few hours to alkaline. There is considerable sediment, very cloudy, and not solid.

Excretion of normal constituents is unchanged.

Carbonate of ammonium is the only abnormal substance which can be detected.

The sediment consists principally of cloudy mucus. Microscopically, we detect mucus corpuscles (young cells) and epithelia from the bladder, in small quantity. After a few hours, small numbers of the crystals of the triple phosphate are found.

This form represents a diseased condition of the mucous membrane, as it occurs in prostatitis after gonorrhœa, and after the introduction of instruments into the bladder and urethra.

(*b*) *Chronic Catarrh of the first degree* is characterized by a wine-yellow, exceedingly cloudy urine, whose sp. gr. is normal, and whose quantity is not increased. The reaction of the fresh urine is acid, but quickly becomes alkaline. The sediment is considerable and cloudy. Sometimes the urine has a peculiar penetrating odor, and the cloudiness, consisting principally of bacteria, is never completely deposited.

The only thing abnormal in the solids is the presence of carbonate of ammonium in small quantities.

The sediment is the same as that of the preceding form, with the addition of bacteria.

This form of urine is found in patients who are forced to use the catheter in order to empty the bladder; in hypertrophy of the prostate gland, paresis of the bladder, and similar obstructions to the passage of urine. In elderly women, who have given birth to many children, or who suffer from any diseased condition of the uterus, this condition is nearly always present.

c. *Acute Catarrh of the second degree* is distinguished from the preceding forms, chiefly by the amount of pus in the urine.

The urine is of a dark wine-yellow color, and is turbid. The turbidity is produced by mucus and pus, while in catarrh of the first degree, the cloudiness is produced by mucus alone. The quantity and sp. gr. are normal, but the reaction is alkaline. The sediment is greenish-yellow, and adheres to the vessel. The only change found in normal constituents is, that part of the urea is changed to ammonium carbonate. Albumin is found in quantities to correspond with the amount of pus present, and carbonate of ammonium is present in great quantity.

The sediment consists of alkaline pus, mixed with crystalline and amorphous earthy phosphates. Blood corpuscles, ammonium urate, and gıeat quantities of epithelium from the bladder are detected with the microscope.

This form of the disease occurs in hypertrophy of the prostrate; after lithotripsy of large and hard

calculi; after the dilatation of strictures; after catheterization, or the introduction of other instruments. Also, after gonorrhœa and acute prostatitis, and, finally, after catching cold, especially depending upon the action of cold and moisture. It occurs in women after operations upon the uterus, or vagina, in perimetritis and pericystitis. It is sometimes observed after the administration of cantharides or other medicaments, and it is said that drinking of badly fermented, so-called "young" beer will also produce it.

d. Chronic Catarrh of the bladder of the second degree produces urine, which is nearly identical with that just described. In addition, as in the chronic catarrh of the first degree, we fine bacteria in the urine.

In the sediment the pus corpuscles are very much swollen, their outlines indistinct and the nuclei distinctly visible; frequently, the latter alone are observed imbedded in an homogeneous, granular mass.

Sometimes the pus is entirely dissolved in the alkaline urine, giving to the latter a syrupy, tenacious consistency.

This form is found in hypertrophy of the prostate gland, in paresis of the bladder and in diseases causing obstruction to the passage of urine.

e. Acute Catarrh of the third degree includes those processes that have been called cystitis parenchymatosa and pericystitis.

Although we are not always able to diagnosticate these diseases from the urine, yet diagnosis is very much facilitated by its examination.

If the quantity of pus is very variable, we can

sometimes deduce the rupture of an abscess of the bladder.

The urine presents the same changes as that of the second degree, with the exception that the purulent sediment does not adhere to the vessel, and that it contains many blood corpuscles.

f. Chronic Catarrh of the third degree is a purulent catarrh complicated by an ulcerative process in the bladder.

The urine is of a dirty brownish-yellow color, has a fecal smell, its reaction is strongly alkaline and the turbidity is produced by pus, mucus and bacteria. The sp. gr. is diminished; the sediment of the same color as the urine, and adheres to the vessel.

The normal constituents are diminished.

Of abnormal constituents, we find a great quantity of albumin, blood coloring matter, ammonium carbonate, and ammonium sulphide.

The sediment consists of ammoniacal pus, mixed with blood and earthy phosphates. Large quantities of bacteria, molecular detritus and single epithelia from the bladder are found with the microscope.

This form of the disease occurs in paralysis of the bladder, and in great hypertrophy of the prostate gland. It is easily complicated by pyelo-nephritis, and symptoms of uraemia or ammonaemia close the scene.

Similar urine occurs in tuberculous ulcers of the bladder and in diptheria.

In croupous affections of the bladder, as they sometimes occur, especially in women, large reddish-white

membranes, which consist of fibrin, are discharged with the urine.

The practicing physician is apt to confound the symptoms of spasm of the bladder with those of cystitis. Examination of the urine alone will make this diagnosis easy.

In spasm of the bladder the urine is generally clear. When it is turbid it is due to the amorphous earthy phosphates which are about to be deposited. The urine is pale, and has a faintly acid or neutral reaction.

In boiling, the urine grows cloudy, earthy phosphates and carbonates are deposited, which are readily dissolved by the addition of a small quantity of acetic acid. Sodium carbonate can sometimes be detected.

Albumin, pus, carbonate of ammonium, etc., are absent in spasm of the bladder.

Calcium carbonate, crystalline calcium phosphate and amorphous earthy phosphates are found in the sediment. Crystals of the triple phosphate and epithelial cells from the bladder are absent.

2.—Neoplasms of the Bladder.

Having discussed the varieties of hemorrhage from the bladder under the head of "Haematuria," it now becomes necessary to state, in detail, the uroscopic signs found in the various kinds of neoplasms of the bladder.

We find the following:

a. Simple fibrous polyps, with a pedicle and hanging into the bladder; they are very rare.

b. Medullary sarcomata; also very rare.

c. Epitheliomata, and

d. Villous, or vascular tumors.

1. *Fibrous polyps* produce symptoms of catarrh of the bladder of the second degree, and only when they ulcerate do we find blood in the sediment.

We are not able to diagnosticate this form of disease, as it does not cause any characteristic histological elements to appear in the sediment.

2. *Medullary sarcomata* produce a similar urine, except in the later stages, when they are followed by catarrh of the third stage. The urine is sometimes of a greenish-brown color and has a very offensive odor. In the sediment is found much molecular detritus, but nothing characteristic.

3. Epitheliomata usually develop very slowly, sometimes producing a catarrh of the second, sometimes of the third degree. The sediment always has more or less of a bloody tint.

Upon microscopical examination we sometimes find numerous peculiar, small epithelial cells (in addition to blood and pus corpuscles), which are occasionally as numerous as the pus cells.

They are small, round or oval, not unlike kidney epithelium. They are sometimes caudate, or have two or three small processes. The nuclei are occasionally very large, several being visible in one cell. Ten or twelve of these cells adhere and form ragged epithelial structures.

Although the diagnosis of epithelioma is not justified by this appearance, any suspicion which may be

held concerning the nature of the disease is very much strengthened by this microscopical appearance.

4. *Papillary or vascular tumors* can always be diagnosticated from the urine.

Two kinds of this form of tumor can be recognized; 1, papillary proliferations (papilloma) of the mucous membrane of bladder, and 2, the true villous cancer.

Parenchymatous hemorrhages are common to both forms; both may be accompanied by catarrh of the second degree, sometimes of the third. Only in the first form may the papillomatous proliferations necrose and fall off, and the patient be restored to health. In the second, cachexia is developed, and the patient dies.

The villous cancer is made up of a more or less soft mass, similar to medullary sarcoma tissue, which grows into the posterior, inferior wall of the bladder, so that a thickening or tumor may be felt by introducing the finger into the rectum. The surface of this tumor is formed by a peculiar villous, proliferating tissue, made up of ecstatic capillaries and a covering of epithelium.

Papilloma of the bladder is confined to the mucous membrane of the bladder. No tumor or thickening of the walls of the bladder can be felt from the rectum.

We can not differentiate these two forms from each other by means of examining the urine—indeed, a villous cancer frequently develops from a papilloma. There are a few points that may make the differential diagnosis possible.

If we find well-developed villi covered over with a

thin layer of epithelium, it is usually considered that a papilloma is present; if the layer of epithelium is so thick that the vessels within the villus can no longer be distinctly seen, we assume that a cancer is present.

But this is of less importance than the detection of intumescence in the walls of the bladder and the presence of a cachexia.

On account of this difficulty of diagnosis it seems fit to discuss both forms together.

In these tumors the urine presents the following changes:

The quantity is not increased, the sp. gr. is normal. The color is that of parenchymatous hemorrhages, and the turbidity is produced by blood and pus corpuscles. The reaction is, usually, faintly acid; only when the tumor becomes larger and the cystitis more pronounced, followed by abundant suppuration, does the reaction become alkaline. The sediment is flaky, brownish or brownish-red, and contains fibers or small ragged bodies of the same color.

The consistency of the urine is that of a thin fluid, but temporary fibrinuria is sometimes observed. This is the only disease that produces fibrinuria in our zone.

When passed, the urine, in these cases, is thin, but in a few minutes it congeals to a gelatinous mass that can not be poured from the vessel. After shaking for some time the urine again becomes fluid, and may then be used for examination. Its color is not always blood-red, sometimes only pale reddish-yellow.

It is always accompanied by tenesmus. The fibrinuria can be explained by assuming that the blood vessels in the mus-

cular layer are compressed by the violent cramp-like contraction of the muscular substance. The veins are compressed more than the arteries, and stasis takes place in the vessels of the villi. If the pressure is very great, rupture takes place, if not, the plasma of the blood is forced out, which afterward coagulates on account of the great amount of fibrin contained in it.

The normal constituents are unchanged:

Albumin and blood-coloring matter are frequently found in great quantity. We must especially notice the fact that the quantity of albumin is greater than would correspond with the quantity of pus and blood, due probably to increased pressure in the vessels. We must be careful not to make the diagnosis of disease of the kidney, in these cases, unless undoubted casts are found in the sediment. Small pieces of villi are apt to mislead the inexperienced observer, being looked upon as casts.

Ammonium carbonate can not always be detected.

When much blood or pus are present it becomes very difficult to see the cancer tissue—indeed, it is then only by chance that particles are observed. It is best, therefore, to select a comparatively clear and colorless urine for examination. Let the urine deposit its sediment, and from this fish out the reddish flakes for microscopical examination.

The sediment consists either of blood only, or of blood mixed with pus. The blood is found in a fluid condition, but coagula are always found. The latter can be distinguished from the villous tissue by their dark red color. We not infrequently find villous tis-

sue inclosed by these coagula. The blood corpuscles are the same as in parenchymatous hemorrhage.

Villous tissue presents itself in manifold forms, according to the reaction of the urine, but we shall be disappointed, if we think to find it as beautiful and characteristic as text-books represent. Entire living villous tissue does not occur in urine; it is only when a catheter is introduced, that we occasionally find it adhering to the openings of the instrument. Necrotic tissue is usually found in the sediment, which may also vary greatly in form.

In the beginning of the disease we find beautiful and characteristic villi (see fig. 14). The villi being necrotic, and their blood vessels ruptured, we rarely find whole blood corpuscles in their interior.

Beautiful villous tissue is most apt to be found in papilloma of the bladder. We are not always so fortunate, however, as to find it. Especially in cancer, with thick epithelial covering, is it impossible to discover villi; as the epithelial layer is beginning to necrose, the individual cells can no longer be discovered. The epithelial layer is infiltrated by pus and blood corpuscles, and is alive with bacteria. Branched structures which represent the stroma and blood vessels are sometimes observed in this detritus.

These histological points are not sufficient for diagnosis, but we find other bodies, with the microscope, which make it positive.

If we examine the necrotic tissue with high powers, we will find parts of the epithelial layer of a brownish color. If the urine is of acid reaction, a closer exami-

nation will show that these parts or spots are made up of crystals of hæmatoidin. If a drop of fuming nitric acid is allowed to flow under the thin slide, a change of color from green to blue and violet will take place. These crystals are characteristic of hemorrhagic tissue, and consequently of importance for our diagnosis.

We also detect crystals which are only found in villous tissue, and therefore pathognomonic. They are small, colorless, circular rosettes, which are only soluble in concentrated acids and alkalies. They are probably calcium oxalate, as they effervesce when treated as calcium oxalate in examining calculi.

When the urine is highly alkaline, the villi are encrusted with ammonium urate and the earthy phosphates. In this case the patient feels as if gravel were passing through the urethra, and is apt to demand an examination for stone.

3.—Calculi of the Bladder.

When stones are present in the bladder, we usually find blood in the urine after exercise, which disappears again when the patient is at rest. Urine passed during the day is more bloody than that passed at night, in contradistinction to other forms of hæmaturia, where the blood is unchanged by time.

Calculi frequently cause cystitis. When small and smooth, as uric acid, they cause catarrh of the first degree; when larger, or of a roughened surface (phosphates, oxalate), they are accompanied by catarrh of the second degree. Hemorrhage into the bladder also depends upon the conformation of the surface.

The reaction of the urine depends upon the amount of catarrh present.

It is of importance to determine whether an affection of the kidney is also present. (See "mixed albuminuria.") If this is detected it is probable that the same process is going on in the kidney as in the bladder.

Determination of the chemical composition of the calculus depends upon the chemical properties of the urine. The amorphous and crystallized combinations found in the sediment form the outer layers of the calculus. The nucleus, in the majority of cases, consists of uric acid (90%).

4.—Diseases of Urethra and the Prostate Gland.

These do not always produce marked changes in the urine. Acute and chronic prostatitis, as well as hypertrophy of the prostate gland, are usually complicated by catarrh of the bladder of the first and second degree. In prostatitis we usually have cystitis of the first degree; in hypertrophy, either of the first or of the second, to correspond with the amount of retention of urine. When the prostata is very much hypertrophied, we usually find spermatozoa in the sediment. It seems that the increase in glandular tissue compresses and destroys the muscular tissue of the ejaculatory duct, thus preventing its closure.

In *spermatorrhœa* the urine is either neutral or alkaline. Upon boiling, it becomes cloudy, and earthy phosphates are precipitated, which dissolve upon the addition of acetic acid (Heller's bone-earth); albumin is not present. Besides numerous spermatozoa, we

find in the sediment, calcium carbonate, crystalline calcium phosphate, and sometimes the triple phosphate. Before making the diagnosis it is necessary to know whether the urine has been passed immediately before an emission or coitus, or not, as we always find spermatozoa in the urine after an ejaculation.

In acute and chronic *gonorrhœa* we find pus corpuscles and single cylindrical epithelia from the urethra.

If the urine does not permit the diagnosis of the origin of the pus, then it will be well to collect the urine in two vessels (Thompson). That passed first will contain all the pus from the urethra — that passed afterward will contain the secretions from the bladder or pelvis of the kidney.

The threads of gonorrhœa, which may be found after normal cases of gonorrhœa, are commonly formed in the accessory glands of the urethra. It is only the very long threads, very rare, that may be formed in the urethra. These threads occur in two varieties — the one, thick, long, and possessing at one end a head-like dilatation; the other, thin and short, and without the dilatation. The former coming from the prostatic portion of the urethra, the latter from Littrés' glands.

Under the microscope they consist of pus corpuscles, mixed with cylindrical epithelia, and imbedded in an homogeneous substance.

In croup of the urethra, small, white, membranous or tubular structures are passed with the urine, together with pus and blood.

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